CAUSE AND PREVENTION OF DISEASE

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TO

MY FAMILY AND FRIENDS

IN WHOM I HAVE FOUND FAR MORE INTEREST

TRYING TO KEEP THEM WELL

THAN CARING FOR THEM WHEN ILL

PREFACE.

The etiology of disease is in a fair way to become a science. This is because every disease must result from knowable causes operating under natural laws that can be determined. I am so convinced of this that I have attempted in this book to systematize what is known about the causes and origins of disease. Whatever virtues it may possess will be outweighed by the revelation that so little is known and so wide a field remains open for investigation.

The book has arisen out of a necessity. Faced with the task of organizing a course in Preventive Medicine I found no single medical work or any small number of them, that embraced all that I thought desirable for an inclusive review of the known causes of disease, where they originated, and what they did. My notes and material collected over many years constitute the basis for this work.

It is becoming increasingly evident that the preventive point of view will not long hence dominate the approach to medical service. For this reason it is necessary to investigate the origins of disease more rigorously and strip them of the confusing pathology and manifestations that make it so difficult to see the simplicity of their beginnings.

In the attempt to formulate my study of etiology I became early indebted to the work of Eugene Lyman Fisk, who classified all etiologic factors in his Categorical List of the Causes of Disease and Ill-health. The present work is a clarification and enlargement of Fisk's conception.

The corollary to setting up a system of causation of disease is a systematic approach toward influencing the operation of effective causes in the direction of health and away from disease. Such would be the Practice of Preventive Medicine. I have put the whole philosophy of prevention in a single phrase, "To oppose or intercept a cause is to prevent or dissipate its effects." It is the possibility of putting the principles of this law into immediate and practical effect wherever and whenever the effective causes of a disease have

been revealed that justifies all efforts at prevention. A disgracefully small amount of present preventive knowledge has been applied in practice. If the pages of this book contain most of the current applications of preventive principles and even hint at a few that the future may hold, I will feel that the attempt has been justified.

The best acknowledgment I can make to those who have assisted in the work is the use of their material. In many instances this has been made explicit in the references but there are others too numerous to mention whose authority has been called upon to validate the statements made in these pages.

I express my sincere thanks to Mrs. Shirley Gage for typing the manuscript and to Miss Stella Hayward for her vigilant oversight and direction of the manuscript and proof in preparation for the press. To my wife I am indebted for constantly reminding me that people primarily want to know how to keep well and for her criticism of the manuscript.

W. H. P.

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CAUSE AND PREVENTION OF DISEASE.

CHAPTER I.

CAUSE AND EFFECT IN HEALTH AND DISEASE.

HEALTH.

Health is a state of relative equilibrium of body form and function which results from its successful dynamic adjustment to forces tending to disturb it. It is not a passive interplay between the body substance and forces impinging on it, but an active response of body forces working toward readjustment. It is a mechanism which deals with initiating forces or energies and by reason of its parts is able to convert them into other useful forms. The parts *through which these forces operate and undergo conversion in the* body are the cells and tissues. Although every living cell in the body retains the primary attributes of living material, a hierarchy has been developed among them which has necessitated the subjugation of certain qualities in some and their exaltation in others; for example, cortical nerve cells have given up their power of reproduction, and muscle fibers have superseded all others in their power of contractility.

Because of this surrender of original rights by the cells and the division of labor which necessarily results in such an organization of dependent elements the integrated mechanisms of response have been evolved.

The fundamental concept of physiology is a responsiveness of the cells, tissues, organs and combined mechanisms to forces of varying kinds and degrees. These forces may originate in the external environment and become translated into the energy activities of groups of cells, or they may be energies exhibiting themselves in one cell or tissue cell group which influence other structures near or far removed from them.

Response to these forces or energies are not haphazard but evidence a definite course and procedure in their activities; the impression is gained that the parts concerned have been "educated" to certain lines of action. Purposeful is an unsafe word to use in

interpreting natural phenomena, but it conveys a certain meaning when applied to the accurate and almost unerring useful responses in human physiology; it raises the commonplace and often sordid functions of the body to the plane of the magnificant, much as do the words in Cannon's title, "The Wisdom of the Body."

There is manifested in each of these adjustment phenomena a tendency toward the preservation of a state of limited equilibrium, but it is not the rigid, static equilibrium of a machine which in itself possesses no means of providing for its growth and development and is incapable of self-repair. Without too strict comparison, it may be likened better to a city organization composed of higher and lower functions that can adjust themselves to meet demands that originate within the city or in external related communities.

Physiologic disturbance is both permissible and necessary in the human economy. There is strong evidence that the very forces which disturb it have been responsible for its evolution; that without the "need" of readjustment and adaptation, the present forms and functions of the body may never have been evolved.

So long as the mechanisms involved in physiologic equilibrium are not pressed beyond their powers of restoration within their established limits, and so long as they retain their ability to dissipate the energies of the factors operating upon them to their own levels of tolerance, it may be said that such apparent instability represents the normal.

It is impossible to define normal more strictly than this. It implies the admission of wide variability in structure and function and in the powers of adjustment within the body. A strict application of normality to the body as a whole would require that the limits of tolerance of each of the functional units of which it is composed must be known. Anatomic and physiologic studies have revealed certain levels of organization and function which have been found so repeatedly in apparently well-regulated bodies that these states have been set as normal against which further observations may be measured. But there is no physiologist or anatomist bold enough to state that these are more than the "apparently" normal.

There are, however, so many of these apparently normal standards, each qualified with its apparently normal range of variability and each remaining within its limits of tolerance or safety, that that body in which all of these flexible standards are satisfied has come to be regarded as a normal body.

A normal, healthy person may be defined, therefore, as one who can retain all of his organs and tissues in a state of efficient function and physical organization against those external and internal forces that are constantly tending to disturb him.

ABNORMALITY AND DISEASE.

Under the average conditions of existence there are few occasions when the balances of the body are tipped to an extent dangerous to efficient functioning. There are many examples of the elasticity and adjustability possessed by the tissues by virtue of which they can respond to stresses and strains beyond the commonplace. Voluntary and involuntary muscles alike can withstand heavy loads put upon them without serious consequences; forced starvation, if not too long continued, does not result disastrously; purgation, sweating and diuresis care for the elimination of toxic substances.

Common experience shows, without resort to scientific evidence, *that the organism can suffer from temporary disorders.* Everyone knows that there are times when he does not feel right; that he is *aware that something about him is not working as well today as it* did yesterday. He may feel "bilious," or "liverish"; be irritable *and jumpy; suffer from peculiar feelings in the stomach or have* palpitations, breathlessness, dizziness and many other common *mild complaints. In many cases there is nothing really wrong with* him and these feelings are brought about by nothing more than *temporary derangements of mechanisms.*

These apparent disruptions in many cases are just within the borderland of normal. Although chemical measurements can be applied to them and the microscope may reveal temporary derangements of tissue elements, these changes are within the limits of normal adaptation.

It is difficult, therefore, to define the limits of the normal and to set up normal standards. It is known, however, that every function can be stressed beyond the limits of its accepted normal; when this is so, the altered function is called abnormal, and the evidence of it is pathology. In so doing an arbitrary, indefinite line has been created between the two states, which is variably called the "borderline of disease," the "limit of safety," the "limit of tolerance" or the "normal limit," each of which implies that the processes of change have been forced to some point which is intolerable or dangerous.

It is upon the determination of this point that the definition of disease must rest. The term disease implies a state manifestly farther from good health than simple ill-health. The man with a "disease" is looked upon as really sick and no longer just feeling badly and out of sorts; pathology is more than tolerable, functional change. Such difficulty of definition can hardly be overcome by the naïve method of resorting to still further undefinable terms, and it must be admitted that disease cannot accurately be defined. Moreover, the modern conception of disease is as a process, not a static entity. The diseases listed in the nomenclatures are no more

rigid and fixed than the processes described within the ranges of the normal, and what are called the classical pictures of disease are complex processes having enough in common to permit them to be labeled for convenience.

Since health and disease are relative states, these terms should be used for convenience of description and not for scientific accuracy. It is desirable, however, to find a workable definition of disease; one which conveys the meaning of what is so far understood and no more. Such a definition must involve the use of terms already defined in arriving at the normal. With this allowance disease may be said to be a state of altered function or form of a part, from which recovery is difficult or impossible, and which for restoration to physiologic equilibrium involves processes or functions which do not ordinarily participate in the physiologic mechanisms responsible for the balances of the parts involved. Pathology is the material evidence of this change.

CAUSE AND EFFECT IN HEALTH AND DISEASE.

The picture behind every observable state of health or disease is one of change. There is a constant flux in the makeup and activity of all cells and tissues so that at no two moments are the arrangements and behavior of parts the same. This change, begun before the union of the parent cells of the organism, continues not only throughout its life, but beyond its death and disintegration. The span of life is thus a continuous flow of energies through a body made up of materials taken from its environment. It creates nothing new within itself but constantly presents its elemental substances in new and complex combinations, breaks them up and returns them to their source. And while the body grows and carries on its processes of building up and tearing down it is being further buffeted by its environment which it cannot escape. It never succeeds in becoming isolated but remains forever a part of its surroundings. The body may be looked upon as a resultant of forces, every force theoretically measurable and the patterns of their interactions predictable.

Notwithstanding the immensity of the problem of knowing all about man, the fact remains that his processes are built-up mechanisms, the beginnings of which are simple actions and reactions between elemental principles, and whose end states are still manifestations of primitive reactions capable of analysis but complicated almost beyond recognition. Every cell, tissue and organ, every operation within and between its parts, every balanced mechanism, every constructive and destructive process in the body is a result of a preceding cause or causes. The chain of cause and effect is tied up with the universal at birth and death, and the body of

man is a falsely isolated interference pattern in this concourse of energies.

Since effective causation can be recognized behind all things in the physical world, so it must be back of every physiologic and pathologic change. To understand physical form and development an attempt must be made to understand why an organism is of such size and build and color; to interpret physiology, adjustments and behavior, the plans and patterns should be known on which they have been built and how they have been called into existence; for the proper interpretation of disease it is essential to have knowledge *of the causes of these abnormal states.*

Scientific medicine has long been probing the secrets of the human body for facts as to the structure and functions of its parts. Out of this study has come a wealth of material, but notwithstanding the phenomenal amount which has been accumulated within the past few decades it is apparent that but a small part of it has been put to work. *Both the science and the art of medicine stand in* great need of finding increased application for this accumulated knowledge.

It is suggested here that a hint as to its use can be found in contemplation of the fact that man is just as much a process as a particle. This means that it will be necessary to think more in terms of change and less in pictures of fixed states; to forget that measures are constant, and relationships consistent; to interrogate every fact as to why it is so, what brought it about, what changed it; to delve more deeply into the mysteries of the why of things and begin to think in terms of Cause. It is in just those instances in which this has already been done that the greatest practical progress in medicine has been accomplished: such, for example, as the benefits which have resulted from the application of the discovery that malaria is not due to a miasma but a specific protozoön carried by a mosquito to which it has become adapted; that locomotor ataxia is the result of infection with a spirochete and that this organism is susceptible to arsenic; that miners' anemia is due to the hookworm; that beri-beri, rickets and scurvy are nutritional defect diseases. It is only necessary to contrast the results in these conditions to the hopelessness that is felt toward the mounting number of deaths from diseases of the heart, arteriosclerosis, cancer and diabetes. A vast amount of information is at hand concerning this latter list and buried in it there must lie much that is available for immediate application. Had Jenner waited for the discovery of the virus of smallpox before applying his principle of protective vaccination the world would still be visited by its plagues; if, after Hansen discovered the leprosy bacillus, nothing had been done to control the disease until it was found out how the organisms passed from person to person many hospitals might still justifiably be called

lazarettes. Not all is known about the vitamins; nor is there complete information as to the true nature of the cause of yellow fever, and yet yellow fever and the avitaminoses can largely be controlled.

THE NATURAL HISTORY OF DISEASE.

Certain aspects of the causes of most human diseases are already known. What is not known about them is their complete cycle of development.

Considered as a process, the development of each disease must be traced from the first forces which acted to bring it about, through the resulting alterations in form and function involved, to its termination by return of the processes to normal or their final disintegration. Such a survey of any disease process would constitute the study of its Natural History.

There is no more reason to deny a Natural History to disease than to the development of the sedimentary rocks or the life cycle of the mosquito. Each involves natural processes; each can be resolved to its simplest terms; through each can be traced the continuous chain of cause and effect. Even the departure from the average course of events in the pathogenesis of a disease can be interpreted as due to factors which have been interposed unexpectedly at some stage of the process.

Thus the variable pictures of so-called disease entities are brought about. All cancers of the same type are not alike and every physician is aware that each case of typhoid fever varies somewhat from the typical description of this disease.

The patterns which result from similar causes cannot be the same unless every conditioning circumstance is the same, and every force which is operating is of the same quality and intensity and acts upon material equally susceptible to it. Such coincidence probably never occurs. What are called classical diseases are designated as such only because the main points of their symptomatology and physical findings correspond to a classical description of a case adopted as a type. All kinds of contingencies may arise to abort a disease and shorten its course, to favor it and produce a fulminating type, to add complications to it, or to cause some of its most cardinal points to be absent. Variability is the rule when disease entities are closely scrutinized, and when the reason is searched for it is found to be the interaction of variable factors.

The typhoid bacillus produces typhoid infection, but every infection with this organism is not typhoid fever. It is also true that typhoid fever or typhoid bacillus infection cannot occur without the typhoid bacillus. Individual and environmental factors of both bacterial organism and human host are the determiners of the final results which will ensue when they are brought together.

The ingestion of mercury may produce irreparable damage to the kidneys but not necessarily so. Other tissues may suffer much more than those of the kidneys when mercury is taken in different dosage and under other circumstances. Moreover, mercury need not be ingested, but may gain entrance to the body by way of the skin or respiratory tract; it may be taken accidentally or on purpose.

It is because of these obviously simple facts that the causes of disease have customarily been divided into primary and secondary causes and that the latter have been further differentiated into contributing, accessory and predisposing causes.

In the specific infectious diseases greatest stress is laid on the specific organism as the primary cause, and in scurvy the lack of vitamin C occupies the same important position. But to consider primary as invariably meaning most important is to acknowledge only one aspect of the etiology of disease. The fact must not be lost sight of that in many disease conditions the secondary, contributing causes may be just as important as the primary cause on the basis that they are just as essential in the whole chain of circumstances that eventuate in disease.

When the Natural History of a disease process is analyzed and the primary and secondary causes are revealed, it is often found *that the final result is due not so much to the activity of the primary* cause as to the intervention of the others, that in all probability the primary cause could not have had any effect without the interposition of the secondary causes. The typhoid bacillus can do no harm outside of the human body, but given the circumstances that permit contamination of a milk or water supply it may cause the disease to develop in a consumer. Milk and water become infected for very definite reasons and it is these which contribute most toward the development of typhoid.

The causes of disease must be pictured as operating before the disease makes its appearance in the subject and they may be working far away from their ultimate victim. Furthermore, all of the causes do not have to act directly on the individual who becomes *affected, as there are often multiple factors that insert themselves* between the earlier operating factors and those that directly initiate the pathogenesis.

Objection will be raised that there can be no disease until the subject of it has become affected. If the whole conception of a disease is to be limited to the stage of pathogenesis this is entirely valid, but the Natural History of a disease expands its etiology far into the ancestry of the diseased subject, or across the town from where he lives, or into his environment at work, at home or at play. The altered physiology and anatomy, the symptoms, signs and pathology, are only the final effects in the far-reaching, complete story of why and how the disease was brought about. This is well

shown in the history of malaria: the malaria parasite is the primary specific cause of the disease, and malaria shows a characteristic symptomatology and pathology when it conforms to type. But a meager knowledge of the Natural History of malaria would result by limiting the study of the disease to the subject of it. Actually the most important causes of malaria and its prevalence reside neither in the parasite nor the host, although each is essential to it; they are outside of and beyond the case of malaria in all of the climatic conditions of the environment, the drainage of the soil, the types of vegetation, the natural enemies of the mosquito and its breeding place, the habitation of the host and the effectiveness of protective devices he has raised against the mosquito.

Many attempts have been made to represent graphically the cycle of development of certain diseases and disease processes, picturing them as chains of development with side-factors introduced here and there to account for certain events. These are at least good cross-sections of certain phases of the disease cycles and as such are valuable contributions to the study of their Natural History. In some, the primary initiating cause manifests itself continuously throughout the cycle and so assumes a highly important position. In others the initiating force is dispelled almost immediately and its effects become in turn further causes and links in the chain. Unexpected side effects are to be found in every case and the course of the disease processes can hardly ever be said to run smoothly. This is so true that the general plan of any disease is a branching side-chain structure.

Throughout this argument the principle of a continuous chain of cause and effect has been maintained as necessary in the explanation of health and disease; it has been held that the causes are familiar, well-known forces in the physical world, and that the first effects are simple biophysical and biochemical responses to them. Because of this it should ultimately be possible to analyze the known facts about each disease and from this analysis to reconstruct its Natural History.

The gaps in this synthesis will necessarily be great in many instances, but in some most of the entire picture will eventually be drawn. Whether or not the course of development of any malady or disease can be outlined in its entirety, it is highly probable that some one or more vulnerable points of its history will be revealed at which it can be attacked and prevented.

CHAPTER II.

THE CATEGORICAL CAUSES OF DISEASE AND PRINCIPLES OF PREVENTION.

The principle of cause and effect permits the corollary, "to oppose or intercept a cause is to prevent or dissipate its effects." As well known as this may be it is the most neglected of all applications in the practice of medicine, and the reason for its neglect seems to lie in the failure to think in terms of cause and to assume too readily that limitation of knowledge makes it impossible or too difficult to try.

On purely logical grounds, nothing need be inevitable and it can be argued that there is no reason why any disease condition *must* develop; that when it does it is in response to a chain of events which directs its course *only* in the direction necessitated by the *given* causes. Any slight alteration in the force or frequency of a causative factor or the addition or removal of factors may produce far different results. It would seem only necessary, therefore, to reveal those places in the Natural History of a disease at which effective measures will block its progress.

All possibilities in the prevention of disease rest on this principle.

A survey of the progress in Preventive Medicine reveals that by far the greatest gain has been made against those conditions brought about by infective agents and nutritional deficiencies. In almost every instance where the specific bacterium has been isolated and its natural history made known, preventive possibilities have been opened up and practical measures against it have been initiated. The disclosure of the rôle of vitamins and mineral constituents of food has made it possible to prevent the diseases depending on the lack of these substances.

But it is obvious that these two classes of agents cannot be the only factors involved in the development of morbid processes. The human environment is much more complex than food principles and bacterial and protozoan enemies. It is apparently because these have been so readily susceptible of analysis and laboratory examination that they have received the favored attention of the medical sciences. The scientific investigator has shrunk persistently from the challenge to evaluate the effects of climate; to all but a few, psychic influences have been so vague and non-analyzable that they are scarcely considered open to investigation, but those

who so ignore them as effective causes exploit their results to the verge of charlatanry; the transmission of hereditary characteristics is too well established to permit any longer its relegation to the interests of eugenics and genetics alone; safety-first measures against traumatism have caught the economic eye of industrial medicine, but the practitioner seldom considers the possibility that static forces operating within the bodies of his patients produce a trauma far more lasting and detrimental to health and efficiency than a bruised thumb.

ENVIRONMENTAL FACTORS IN DISEASE.

Viewed in its entirety the environment is seen to contain most if not all of the intiating factors of disease. This statement must be qualified because it is still impossible to state with certainty that there are not causes which appear to arise within the body itself, but whose antecedents are so remote as to be beyond practical consideration; such, for example, as the unexplained failure of tissues to reach their full biologic level.

It is only when disease is looked at too narrowly that the error is made of ascribing its causes to happenings within the diseased organism. The clearer but more difficult picture is obtained by pursuing events until the external environment is reached and the primitive simple factors are revealed.

The analysis of environment must ultimately be the key to the knowledge of the origins of disease. The cell, tissue and organ reactions within the body may be studied, but the original causes of disorder must be sought for outside the organism.

CLASSIFICATION OF ETIOLOGIC FACTORS.

From the desire for a complete understanding of the Natural History of disease the need arises for a systematic survey of etiologic factors. The more recent text-books on general and preventive medicine mirror this need by arranging their material under headings according to their etiology, and the new Standard Nomenclature of Disease, makes etiologic classification obligatory. These uses of etiology are for immediate application and must necessarily allow for gaps in knowledge; the text-books, by retaining section titles such as Diseases of Unknown Cause or Unclassified Diseases, and the Nomenclature by allowing sub-divisions under which doubtful causes and mechanisms may be retained.

In setting up an etiologic classification on which the principles of prevention may be based there is no obligation to allow for any doubtful factors unless they are such as to be still unknown in the

physical world. This is because all forces capable of producing disease *can* be categorized. It is possible to erect a schema of classification of causes which shall be inclusive enough, within its categories, to embrace every known cause.

Fisk[1] simplified the classification of the causes of disease by including them under ten categories: Heredity, Infection, Poisons, Food Deficiency or Excess, Air Deficiencies or Defects, Hormone Deficiency or Excess, Physical Trauma or Strain, Physical Apathy or Disuse, Psychic Trauma or Strain, Psychic Apathy or Disuse. In this list Fisk has satisfactorily embraced all existent and predictable causes, but in doing so has resorted to alternatives of action in some categories and permitted overlapping between others. As examples of the latter the inclusion of all of the factors of "Air Deficiencies or Defects" under one category has separated the physical aspects of air from the physical factors covered in another category; food deficiency or excess may be taken to mean anything from the lack of vitamins to faulty habits of eating. It is not argued that either of these extremes is not a cause of disease or ill-health, but it is not permissible to place a fundamental cause like a vitamin deficiency on the same basis as a process such as the method of taking food. The latter may be discussed under food deficiency, but it is not a primary categorical factor.

Objection may be raised against the causality of the "Hormone Deficiency or Excess" category on the ground that the internal secretions do not of themselves initiate changes but over- or underfunction as a result of some antecedent factors. Although little is known of the reasons for their malfunction, there seems no reason why they should be predicated an autonomy which is denied other tissues or organs. When a hormone does fail the cause will be found in one or more of the other categories.

Disuse may permit an abnormal state to be brought about, but it is not the prime mover of the process; it is not only the absence of use but is evidence that customary activators are wanting or that inhibitory factors have been introduced. Broadly, disuse may be looked upon as an opportunity for other factors to operate, but this is not within the limitations of a basic category and the term should be dropped. Apathy is entirely too inadequate and vague in either its physical or psychic connotations to be used as an explanation of any result, and may be objected to under the same argument that was brought against disuse.

The following Categories of the Causes of Disease have been selected as more nearly satisfying the demand that each category shall contain all factors that operate in the manner indicated by

[1] Fisk, Eugene Lyman. Ann. Am. Acad. Political and Social Sci., Philadelphia, vol. 145, Pub. No. 2323, 1929.

the titles of their respective categories and at the same time exclude all factors in other categories:

Category I. Inherited Factors.
Category II. Defects of Nutritive Elements.
Category III. Exogenous Chemical Agents.
Category IV. Physical Forces and Energies.
Category V. Vital Activity of Invading Organisms.
Category VI. Psychobiologic and Bio-social Influences.

The terms used in the titles of these categories reveal that they are selected on the basis of their modes of action. Thus each one acts in a different manner than all the others, provided the point is not stressed that all depend eventually on ultramolecular forces. The manner in which chemicals act on the physiologic mechanisms is different from the way in which inheritance factors are transmitted, and quite unlike the action of stimuli arising within the bio-social factors; food elements, although chemical in nature, are only those substances which can become useful metabolites, and their selection as a category depends on their utility and not on their chemical action

The categories therefore embrace the primary etiologic factors in disease; they contain the starting points from which all subsequent effects and mechanisms arise. Without these factors there would be no disease for the consequences of their activities would not follow, and it is these very phenomena which constitute the developmental processes of disease. To follow any influence from its origin in one of the categories through all of its effects outside of and upon the body, is to trace the Natural History of the disease conditions which result.

An important factor to be considered in the operation of a categorical cause is the directness of its action. This may be simple and direct or complicated and remote. It may act immediately on a body function without the intervention of any other effect, or it may start a long chain of events which are circuitous and indirect until finally, through some terminal event it exerts its influence on the body. Simple traumatism exemplifies direct action of a physical force and the circuitous history of some of the animal parasites as they become involved in many secondary processes represents indirect action on the part of an invading living parasite.

Most of the predisposing or secondary causes of disease are found within these chains of circumstances and they are noticeably lacking in the titles of the categories for the reason that they are not initiating causes They are not primary effective causes as the term is commonly applied; they are mechanisms or operations or circumstances under which the effective causes act. Thus, occupation is not a cause for it is only a circumstance under which the cause and

its effects occur and it may be broken up into many categorical factors. Race and sex, although generally referred to as predisposing causes, are the results of the transmission of inheritance factors. In the same way climate is a complex inclusive term which embraces many kinds of physical force and energy.

Nevertheless, the secondary causes are highly important concepts, for they show how and where groups of events and circumstances occur and thus bracket off quasi-isolated sections of natural histories. They give important clues which in many instances have revealed the outstanding links in the chain of circumstances.

THE CHAIN OF EVENTS IN HEALTH AND DISEASE.

On the principles outlined it can be seen that the prime movers (categorical causes, initiating forces) are relatively few in number compared to the multiplicity of their effects. When one of them comes into action, its force is exerted on other agents and factors which react to it. This may be exemplified in the way the cue ball in pocket billiards breaks up the triangle of balls and disperses them in all directions although the cue ball itself may strike no other ball except the one at the apex of the triangle. What happens to the other balls depends entirely on the way in which they were set up and the angle of incidence and force with which the cue ball set them in motion. The final result shown in the way all the balls eventually come to rest, is theoretically perfectly predictable. And so, provided the set-up could be known of all the factors concerned in the origin and development of a disease, its course could be predicted to a certainty. But intervening influences, not a part of the original set-up, may come in to disorganize the entire operation just as an onlooker might reach out his hand and deflect any ball while it is in motion on the table. In actual experience, therefore, it is seen that a single initiating cause may, under variable circumstances, produce an almost infinite number of possible effects, and it is for this reason that there occurs such great individuality as is found in disease pictures, multiplicity of symptoms, variable pathology, and uncertainty of prognosis.

PRINCIPLES OF PREVENTION.

Acting on the assumption that obstruction or interference with a cause will alter its effects, it is possible to apply this principle in the prevention of disease by deliberate efforts toward affecting the circumstances that determine the course of events. Thus, if contamination of a water supply is the occasion by which pathogenic organisms enter into a community, purification of the water will prevent those diseases due to particular causative agents in the water. In this instance a single effort has created a barrier against

many possible water-borne agents and prevented the diseases which they might otherwise have produced. Such broad measures as these are termed blanket measures. Food and drugs acts, quarantine regulations, sewage disposal and personal hygiene are procedures of the same nature.

Reverting to the example of the game of pocket billiards it is to be noted that the effect of the cue ball can be altered by disarranging the alignment of the balls in the triangle. If a corner ball is separated from its fellows by even a fraction of an inch the distribution of the forces in the organization of balls will not now be the same as before when the cue ball sets them in motion. Since the result in this instance is largely limited to the changed effect on the corner ball alone, the interference has been an individual effort applied only to that particular ball. Preventive medicine applies this principle in its individual measures directed toward the prevention of disease in the units of an organization. Quinine prophylaxis against malaria and specific immunizations act by permitting the agent to approach the organism, but preventing its effects on a particular function of the organization by altering the set-up in that function. Such measures are called specific measures.

From the foregoing possibilities it is evident that what is now needed for the furtherance of the prevention of disease is a more complete knowledge of the Natural History of disease. Although a complete outline of the history of any disease is not essential, it is desirable because it opens up more probable points at which the causative factors or the circumstances under which they are found, can be attacked.

Expediency has determined many of the past preventive efforts and will continue to do so for a long time to come. In the meantime there can be little excuse for continuing with the present haphazard measures, especially in those diseases due to categories other than infective agents and nutritional defects. The heavy toll of the so-called degenerative diseases or those which appear concomitantly with advancing age is a direct challenge to find out more of their historic development, to realign knowledge of their progression into as complete a story as possible, and to look broadly at the revelations that this may show.

This calls for a change of attitude toward disease. It means that the old static idea of disease must be cast side and that disease must be looked upon as a constantly changing chain of events, not inevitable, and controllable by conscious effort against it.

The success of prevention lies, therefore, in a complete understanding of the nature of the causative factors in each category and an analysis of their modes of action and results.

CHAPTER III.

CATEGORY I: INHERITED FACTORS.

THE MECHANISMS OF INHERITANCE.

THE human being is conceived favored with the assets and burdened with *the liabilities of its ancestors. In this statement of* inheritance is found all the hope of human betterment and the despair before the tenacious drag of race faults; for man is born of the continuous stream of germ plasm which has carried his inborn traits through the generations, unaffected, so far as is known, by the manner of living of his forebears. All of his potentialities, and every direction of his development, are present in that one-celled organism, the result of the joining of two others, each of which has brought to the union the traits and characters of its own ancestral cells.

The individual stands at a cross-roads, a receiving and dispatch agent of heredity. From the incoming lanes he receives all of the goods forwarded him by other agents of his line and after due delay, transmits them onward and unchanged to his progeny.

The original package which he receives is microscopically minute, its contents as multitudinous as the sum of every character of his hair and eyes and body type, and all tissue and organic elements of which he is composed. Retaining the simile, the contents are the inheritance factors, the forwarding process is heredity; what is known of the structure of the one and the mechanism of the other is at present a good scientific guess.

Categorically, the inheritance factors are primary causes; the individual had nothing whatever to do with them either in their particulars or in the aggregate. Nor was he even an individual until the organization of the factors and the vehicle which carried them had been completed. Before him, his traits were existent but dispersed through his ancestors, after him they will again be separated according to the number and behavior of his children. But from the moment that the ovum and spermatozoön which produced him have united and gone through the first processes of fertilization and consummated the final arrangements of cytoplasm and nuclear elements in keeping with his species, he is *himself*.

From this starting point, the individual is on his own responsibility, free to do with his inheritance as he pleases, but restricted to the use of those inheritance factors handed down to him.

It is no longer supposed that inheritance factors are the gemmules postulated by Darwin as real entities or microscopic imagos from which future characters emerge but are "determiners" or, genes; molecular aggregates that hold potentialities for determining the structure and organization of materials built under their directing influence.

The genes are influences, or determining factors, which act by virtue of their potentialities, as prime movers in ontogeny. Their *sum determines the individual and if one of them be absent or* another added the developing organism will not be the same. It is from this, and the fact that the genes are dispersed through a divergent ancestry and brought together in an infinite number of combinations through bisexuality, that the human race escapes the monotonous similarity of the amœba.

The mechanisms by which the inheritance factors are transmitted to and converged in the individual, and the processes and operations in which they are involved are so important to a clear understanding of their influence in disease that they must be reviewed briefly.

CHROMOSOMES AND GENES.

The germ cell is a complex organization of many readily demonstrable structures some of which have been shown to be directly concerned in the process of preserving the continuity of germ plasm through successive generations while others are more involved in cellular development. Although it cannot be said with certainty that the dividing line between these structures and their functions *is as sharp and fast as it has been depicted, there is little doubt* that some of them in certain phases of their activity are definitely involved in the mechanisms of heredity. Outstanding among them are the chromosomes, visible short-looped or comma-shaped bodies appearing in the nucleus most clearly during the processes of cell division. Their number varies with different species of cells so far studied but is constant for each species—thus the human germ-cell contains 48 chromosomes arranged in 24 pairs.

Because of their consistent behavior in all observations on reproducing cells and on account of the close parallelism between their known activities and the results obtained in experimental genetics, the chromosomes have come to be accepted as the structural basis of inheritance.

With the improved technics of cytology, the chromosomes have been found to possess an internal structure of even further fundamental importance to heredity, that is, the chromosomes contain aggregates of particulate bodies, called genes, which are the physical units of inherited characters. The genes are arranged in definite patterns within the chromosomes and because they carry with them

in that form the entire inheritance of the race to the individual their alignment is called the "genotype pattern." It is apparently the pattern which determines the individual and not simply the qualitative and quantitative characteristics of the genes. An interesting comparison has been made between the arrangement and interaction of the genes and the relationships between the elements in the higher chemical compounds. Carbon, hydrogen, nitrogen and oxygen can be combined in almost innumerable patterns to produce a wide variety of complex organic compounds, a result not only of the number of elements combined but the way in which they come together. The genes with their even greater number have combined to form as many patterns as there have been human individuals on the earth for, with the exception of identical twins, no two patterns are alike.

It is not to be supposed that there is a gene for every character any more than that a gene is a character in miniature for some of the simplest characters are determined by the interaction of many genes. The exact nature of this interaction is not known but indications point to molecular rearrangements and affinities.

In the reduction division of the germ cells involved in biparental reproduction, the chromsomes are reduced by one-half; in the ovum one-half is retained and the other half is lost in the formation of the polar bodies; in the sperm, each half is distributed in new spermatozoa. When fertilization occurs the remaining half portion of the chromosomes in the female ovum unites with the half portion of the male spermatozoön and the resulting zygote has thus restored it in the full complement of chromosomes for the species. Since the chromosomes of the maternal and paternal cells contain genes as different in their patterns as their own ancestry necessitates, it can be seen how this mechanism not only preserves a continuous line of chromosome-gene material but permits a reshuffling of the pattern with each individual formed.

Thus there is found in the reduction division and maturation of the ovum and the sperm, in the process of fertilization, and in the subsequent division of the zygote, which ultimately ends in the formation of new germ cells, a continuous mixing and segregation of the elements of both parents. It is believed that the integrity of the parental genes is never lost even in the conjugation of the chromosomes and this is partially confirmed by recorded instances in which the maternal and paternal chromosomes have been visibly differentiated throughout the process.

Mendelian inheritance, which in all probability is the only form of inheritance in man, depends therefore on the physical independence but functional interdependence of genes. Every cell contains an equal number of genes derived from each of its parents and these

genes, remaining discrete and independent in form, interact with and influence each other to bring about the germinal organization of the individual.

MATURATION DIVISION.

The total amount of chromosome material is maintained constant in matured germinal cells by the process of reduction division in which the chromosomes are numerically halved by equatorial division; the quantitative equality of biparental germinal material in the germ cells is assured by longitudinal splitting of the chromosomes. The former process, or first maturation division, may be pictured by visualizing a set of small thread-like bodies arranged more or less in a circle within the nucleus of a cell which, as they are watched, slowly come into motion, and dividing, form small U-shaped loops one-half of which go to one pole of the cell and one-half to the other. The cell then divides between these two groups leaving an equal number of chromosomes in each new cell. In the second maturation division which follows soon after the first, the thread-like bodies are similarly arranged but each chromosome now splits lengthwise into two. This split is not along an accidental line but a persistent line of cleavage between the maternal and paternal chromosome material of which the chromosome was originally composed. After this split, one-half of the thread goes to one pole of the cell and the other half to the opposite pole and the cell then divides between them, thus giving each new cell half maternal and half paternal material. The genes within the chromosomes must necessarily share in this division. Later, when synapsis or conjugation of the chromosomes occurs after fertilization of the ovum, the maternal and paternal elements which are similar in size, shape and function, in the two germ cells unite with each other to form homologous pairs. Because the genes contained in the chromosomes are involved in the process and because their distribution in character and quantity was equal, and like groups conjugated with like, the genotype pattern is maintained.

DOMINANCE AND RECESSIVENESS.

The existence of familial and racial traits and characteristics is evidence that these are carried through the mechanisms of inheritance but it also reveals an apparent inconsistency of transmission for all children do not show all characteristics of their parents and all members of a race are not equally endowed with the characters of the race. That this inconsistency is more apparent than real has been proven by studies in experimental and statistical genetics and is explained by the theory that some hereditable characters are dominant over others and that hybridization or mixture of race types brings together dominant and recessive characters in variable

mixed patterns. Recessive characters are not lost but are temporarily submerged and may reveal themselves when segregation permits them to appear in new combinations in which the dominant character is absent. It must be remembered that the appearance of a recessive character may not necessarily indicate the absence of a dominant character (presence-absence theory) but the recessive unit may itself be a positive quality. There thus appears to be a form of antagonism between dominant and recessive characters. Unit characters occur in pairs called allelomorphs which can be segregated in the offspring. When the allelomorphic pairs in a germinal cell are made up of similar units in respect to a given character the cell is called homozygous; when they are opposites, the cell is heterozygous.

When an individual produces germ cells the paired characters separate so that each germ cell contains only one of two contrasting characters. This occurs even though the germ cells were produced by a hybrid in which the characters were mixed. This is the "purity" of the germ plasm and is dependent on the principle of the segregation of allelomorphs.

To reverse the picture, if two germ cells, identical in respect to any unit character, unite, the result will be a homozygote or pure-line individual; should the union be between two cells bearing contrasting unit characters the product will be a heterozygote. Pure dominants will produce only dominants in the second generation and pure recessive only recessives. If two hybrid parent cells with identical dominant-recessive make-ups of a unit character unite they will produce an equal number of dominants and recessives and a "mixture" of dominant-recessive offspring.

The proportions of each is shown in the following diagram of possible combinations from such a female and male of similar hybrid germ-plasm structure in respect to the same unit character D-R:

HYBRID INHERITANCE

D = dominant

R = recessive

Germinal cells

	Paternal ovum		Maternal ovum.
Hybrid ♂	D		R
Hybrid ♀	D		R
	Sperm		Sperm
F_1 or	DD	DR DR	RR
Mendelian ratio	1 :	2 ·	1
Apparent ratio	3		. 1

In the combination DR, the recessive character will not appear because of the presence of the dominant D, therefore, in all of the

offspring the dominant will become apparent in the ratio of 3 to 1 to the recessive because D appears twice in the DD offspring and once in the DR and not at all in RR, and since RR contains no D, the recessive R may show itself in this offspring and in it alone.

LINKAGE.

From the picture presented of a germinal cell possessing a specific number of chromosomes each of which contains a hereditary assortment of character determiners, and from the behavior of its chromosomes in division and conjugation, it might be expected that the genes within them would tend to be passed around in groups. That this actually occurs has been shown by Morgan and his co-workers in their observations on mutations in *Drosophila* (the pomace fly), in which they noted that with the appearance and continued inheritance of these sports certain characteristics were transmitted in groups or associations. From this and earlier studies on sex by others has come the acceptance of the principle of *linkage*. In brief, linkage is the tendency to continuous association of a group of characters within a chromosome; its explanation goes back to the principle of the integrity of the determiners throughout the conjugation and segregation of the chromosomes. Thus the older idea of blending as a "melting pot" has given way to the conception that blends are not irrevocable fusions of unit characters transmitted as such to the offspring but are temporary unions of factors which can be segregated in new germ cells: this reveals the reasons for submersion and reappearance of family and race resemblances.

SEX CHROMOSOMES AND SEX LINKAGE.

Of special importance to medicine is the association of unit characters in certain chromosomes which have been distinguished as the sex chromosomes. Cellular analyses have shown beyond doubt that the chromosomes in the sex cells in man are not all similar, but that there is one chromosome which is morphologically distinct from all the others. In male germinal cells or spermatogonia this odd chromosome, now called the X-chromosome, passes during reduction division into one or the other half of the divided cell leaving the other half without it. One-half of the spermatozoa are therefore *simplex* as to the X-chromosome, that is, there is only one X, and the other half is *nulliplex*, without the X. Female germinal cells contain two X-chromosomes, and are *duplex* in respect to it. When these cells reduce their chromosomes an X goes into each half so that all ova are simplex. The duplex state is the one which develops into the female. If therefore an ovum (X-containing) is fertilized by a simplex (X-containing) spermatozoön a duplex (X–X) female will develop; if an ovum (X-containing) joins with

a nulliplex (non-X-containing) spermatozoön, a simplex (X-) or male will be the result.

It is not necessary to assume that all subsequent sex characteristics of the individual are the result of this X-chromosome, since environmental and hormonal factors may determine them in part but it is certain that some determiners in the X-chromosomes are responsible for the direction of sex character development.

As with the other chromosomes there is a tendency toward permanent association of groups of unit characters in the sex chromosomes. These characters may not all have specific relations to sex development but are always found in association with them. Such non-sex characters which appear or disappear in accordance with the movements of the X-chromosome and its duplex, simplex, or nulliplex condition are called sex-linked characters. Several *important disease conditions are determined by associations of this* nature and will be discussed more fully later.

CROSSING-OVER OF CHROMOSOMES.

In the description of the process of segregation it was stated that each chromosome split lengthwise along the line of cleavage between the maternal and paternal elements. Careful analysis of the transmission of linkage groups by Morgan revealed that they did not always behave as pure groups confined to one or the other side of the line of separation in the chromosomes, but that they occasionally became mixed. That is, some characters of the maternal side were transmitted with the paternal characters while at the same time some paternal characters appeared along with maternal elements of the same group. It appeared as though there had been an interchange of maternal and paternal characters at some point or part of the chromosome. This Morgan showed could occur if during some stage of synapsis the maternal and paternal threads should become twisted about each other and then in reduction division separate as usual along the long axis. It would then be possible that those genes located between any two twists of the thread would have crossed-over and interchanged. That this twisting actually occurs in synapsis when the threads are long and thin has been demonstrated, and Morgan's cross-over explanation of the formation of new and mixed groups appears to be well substantiated. Moreover, the threads may twist at several points and result in several cross-overs in the same chromosome. So accurately has this been studied that from these observations it has been possible for Morgan to map the location of many of the genes in the chromosomes of *Drosophila*.

Although crossing-over seems to have complicated the pure transmission of linked characters it has actually given further proof of linkage and has also confirmed the fact that genes do not blend

but remain discrete and separable in every mechanism of inheritance so far observed.

This short survey of the mechanism and physical basis of heredity should point clearly to the reason for selecting inheritance factors as categorical causes. So far as the developing individual is concerned, there is nothing in himself further back in his existence than those factors which have converged to make his beginning, and if any of them possess potentialities for harm or the prevention of harm they can be looked upon as causes of the developing state. That the end results may be due to the addition or removal of other causes operating in other categories does not detract from the primary influence of these inherited factors.

HEREDITARY CONSTITUTIONAL TYPE.

The sum total of an individual's make-up, developed under the influence of his environment in a direction dictated by his inheritance, is called his *constitution* or *habitus*. Within the limits of his ability to change his environment or to adapt himself to it he is capable of many lines of development of his phenotype or somatic organization, but always there is beneath this a more basic framework insusceptible to changing conditions of development or environment and called the genotype, inheritance type, or hereditary constitution.

Although the concept of constitution has long been recognized and made familiar in the expressions "general make-up," "personality type," "individuality," and others of similar nature indicating uniqueness of the individual, it is only with the discovery of the physical basis of inheritance that its true meaning has been made clear. It is now known that the phenotype or realized individual is unique because his genotype pattern is unique and not only because his food and environment are different.

Constitution studies must recognize the full import of the inherited basis. To say that it is too difficult to analyze in the individual is to ignore the one most important fact about man.

In order to recognize the genotype pattern in a given individual it must be known how and where to look for evidence of it in his entire constitution. At present this can only be done on broad principles for the changes from the original pattern brought about by environmental influences cannot yet be determined with any accuracy. But it is possible to see beneath the sum total of an individual's make-up, certain patterns of characters which when grouped together form resemblances in race and family types, sex-character associations and, according to Draper,[1] disease types. These

[1] Draper, G., Human Constitution, Philadelphia, W. B. Saunders Company, 1924.

partial constitutions or pseudo-isolated genetic patterns have long been recognized in clinical medicine and were formerly held in much higher esteem as aids to medical understanding of patients than now. There is a great probability that many of the grouped characteristics which Draper has revealed in his studies on constitution and disease are linkage groups and if this be so a wide field of study is opened in the investigation of those tendencies and resistances to disease which seem to go along with them. Outstanding among these are his correlations of anatomic types with gastric ulcer and gall stone disease.

His findings in these two contrasted types are tabulated as follows:

Measurement.	*Gastric ulcer.*	*Gall-bladder disease.*
Gonial angle (average) (Angle between horizontal and ascending rami)	120°	112°
Palate	Narrow and deep	Broad and shallow
Incisor teeth	Long and narrow	Short and square
Face	Long and narrow	Broad and short
Interpupillary distance	Relatively distant	Relatively close
Thorax	Relatively short antero-posteriorly	Large in all dimensions
Subcostal angle	40°	50°
Pelvis	Narrow	Broad (males relatively wider than females)
General Type males	Slender and masculine	Fat and tend to feminism
	Mostly males	*Mostly females*

Other observers have recorded similar correlations between anatomic measurements, body characteristics and disease. Bean[1] *and Bryant[2] have correlated intestinal length with morphologic* human types and disease tendencies; Beneke[3] described certain constitutional inadequacies in persons with small aortas; and Näcke[4] found tabetics to conform mostly to the asthenic, long-chested, long-legged types while paretics were largely sthenic, short, and stockily built.

In the above findings it is to be noted that the anatomic and morphologic criteria are largely of the same order as those used in general biology for species determination. That man has specific characteristics cannot be denied and there is a possibility that some of these correlations between morphology and disease are due to

[1] Bean, R. B.: Morbidity and Morphology, Bull. Johns Hopkins Hosp., 23, 363, 1912.

[2] *Bryant, John. The Carnivorous and Herbivorous Types in Man, Boston Med.* and Surg Jour., 172, 321, 1915

[3] Beneke, F. W.: Die Alterdisposition, Marburg, 1897.

[4] Näcke, P.: Allg. Ztschr. f Psychiat., 50, 557, 1899

constitutional linkage. That they are strictly genetic in the sense that there is a tendency to disease determined by gene pattern and relationships, and brought out by environmental influences, is not so certain and remains an open question. The danger of assuming that the disease is the result of the morphology is great and any reasoning from the facts can go no further than to say that there is a correlation between them and that possibly the morphology *may* be *one* factor in the determination of the disease.

There is a school of thought that regards inherited constitutional types as due to hormonal or endocrine disorders. This trend has sought to explain everything from race type to individual peculiarity of temperament, with, it must be admitted, but little regard for scientific truth and accuracy. There is no real basis for assuming that because an apparently normal person presents morphologic peculiarities that resemble those of patients with acquired endocrinopathies, that the apparently inborn type is caused by persisting imbalance in the glands of internal secretion. But since such resemblance does exist and these types tend to appear in families, it may be true that they are hereditary constitutional types which depend on a genetic pattern in which glandular inheritance plays an active part. Not that they are disease states but that they represent normal variations in the balances of all physiologic mechanisms of which the endocrines are a part. This is quite different from inheritance of endocrine disorders, which will be discussed later.

PREDISPOSITION AND DIATHESIS.

A group of disease conditions even more generally associated with hereditary constitution is represented by those due to the so-called "diatheses," "tendencies," "susceptibilities," "pre-dispositions," and various forms of "constitutions." Ryle,[1] the most recent of those who have attempted to define diathesis looks upon it as a "transmissible variation in the structure or function of tissues rendering them peculiarly liable to react in a certain way to certain extrinsic stimuli." He thus assumes dual causation, part hereditary and part environmental, and his definition appears to conform closely with what is known about diathetic conditions. Discussion in the past has centered largely around the question as to whether it was the disease or a liability to the disease which was carried in the individual, or a tendency to the manifestations of the disease. Ryle's definition brings the opinions of the old and new schools together and places the whole matter within the realm of genetic investigation. The revival of interest in heredity and disease manifests

[1] Ryle, J. A: Physical Type and Reaction to Disease, Guy's Hosp Gaz, 40, 546, 1926

itself in the large bibliography of medical articles dealing with the elements of heredity in such diseases as cancer, diabetes, arteriosclerosis and epilepsy, and in a group of much less tangible entities such as resistance or susceptibility to specific infections, allergic hypersensitiveness and idiosyncrasy to certain drugs and poisons.

The more evident the environmental factors become in the causation of disease, the more difficult it is to prove a hereditary basis in any condition where it is suspected. There is a long list of abnormal states which the physicians of pre-bacteria days believed to exhibit familial hereditary tendencies. With the discovery of the rôle of bacteria, vitamins and other environmental influences in the production of disease, these "hereditary tendencies" were largely discarded, because it was felt that the newly discovered causes were adequate explanations for the whole picture of disease. Subsequent studies have shown how wrong they were in many instances for the revealed causes have not proven to be so satisfactory and complete as had been assumed.

Many competent authorities now insist that cancer, diabetes, and many other diseases, as well as liabilities to certain infections and increased resistance to others have a hereditary constitutional basis, and yet the evidence rests on but a few facts which are highly *suggestive but not proven.*

When family incidence shows itself repeatedly in investigations on a given disease it is a potent argument in favor of heredity, and especially so when a careful analysis of all environmental etiologic factors fails to account completely for its origin.

The suspicion of an inherited factor has long been expressed by the layman when he says that a family has a tendency to "delicate throats," "poor hearing," "weak eyes," "stomach weakness," "consumption," and "kidney trouble."

It is obvious that such observations cannot be relied upon but evidence is accumulating that there may be some scientific truth beneath these tales and they cannot be dismissed too readily. On a wider basis than the family there is evidence that there are race *liabilities and resistances to disease which are not entirely due to* differences of environment or exposure. Such conditions are as divergent in their etiology as tuberculosis and diabetes and there are competent scientific authorities who support the belief that there is an inherited element in them.

When it can be shown that there is a high correlation between any manifestations of disease and a known hereditary constitutional factor, the argument in favor of heredity becomes even more impressive. Thus it has been shown by the studies of H. and L. Hirschfeld[1] on a large series of parents and children that there is a significant

[1] Hirschfeld, H., and Hirschfeld, L., Klin Wchnschr., 3, 2084, 1924; Lancet, 2, 675, 1919.

correlation between blood groups and immunity or susceptibility to diphtheria as determined by the Schick test. Blood groups have been shown to be hereditary through both family and race studies and are therefore inherited constitutional factors. That such a definite phenomenon as resistance (or lack of resistance) to a specific bacterium is related to heredity is presumptive evidence that correlations of the same order may exist in other infections.

Garrod[1] is insistent that there are in-born factors, largely of a chemical constitutional nature, in some of the errors of metabolism and the hypersensitiveness to various foreign proteins and other chemical elements such as drugs and vegetable and animal poisons.

Thus, heredity, although unproven, must be held suspect in the groups of diseases and morbid processes so far discussed, but the evidences in favor of and against it are so manifold that no attempt can be made here to detail them.

If heredity can eventually be shown to be operative in questionable cases the inherited factors must conform to the mechanisms of heredity. This means that further study on these diseases will have to take into account the part played by linkage, crossing-over, sex-linkage and all of the complicated processes of hybrid inheritance, and the transmission of dominant and recessive characters. Also, many of them will probably be found to be due to multiple factors and therefore dependent for their appearance on the entire genetic pattern, or by linkage with larger patterns on particular chromosome inheritance.

HEREDITARY DISEASES.

In contrast to these suspected inherited trends there are a number of abnormalities of structure and function and some few disease entities which have been proven to be definitely hereditary in nature They all exhibit some one or more of the criteria necessary to establish their hereditary character, the outstanding being the phenomena of dominance and recessiveness and sex-linkage.

Owing to the difficulties encountered in the study of inheritance of disease in man, due in part to the incompleteness and unreliability of geneologic records and part to masked dominance, skipped generations, multiple variants, poly-hybridization, and general smallness of human families, it is impossible to be too definite in asserting that any disease shown to be hereditary is transmitted as a dominant or a recessive.

In a few conditions there is little question as to their mode of transmission and many authorities are in perfect agreement concerning them. This is especially true of the structural defects, some

[1] Garrod, A. E. The Inborn Factors in Disease, Oxford, Clarendon Press, 1931.

of the abiotrophies, and those conditions which are sex-linked. These diseases have been followed carefully through many family lines and their behavior is unquestionably established. Others *which have been traced through many families and generations,* still remain in doubt, not as to their hereditary nature but as to how they are transmitted.

The following table of hereditable diseases and pathologic conditions has been compiled from many sources in an attempt to show the current status of opinion on the subject. Doubt as to the manner of transmission is shown by the inclusion of some conditions under both dominant and recessive headings, and those in which inheritance is questioned or suspected are so indicated.

INHERITED PATHOLOGIC CHARACTERS IN MAN.

Dominant.	*Recessive.*
Hereditary cataract	Albinism
Night blindness (when not sex limited)	Pigmentary degeneration of retina
Brachydactyly	Alkaptonuria
Polydactyly	Hereditary epilepsy
Syndactyly	Hereditary feeblemindedness
Symphalangy	Hereditary insanity (dementia præcox and manic depressive)
Exostoses	Hereditary alcoholism?
Hereditary fragility of bones (Fragilitas ossium)	Hereditary criminality?
Diabetes insipidus	Hereditary hysteria?
Huntington's chorea	Multiple sclerosis
Achondroplasty	Friedreich's disease (hereditary ataxia)
Keratosis	Ménière's disease
Epidermolysis	Chorea
Hypotrichosis (and edentate condition)	Thomsen's disease (myotonia)
Diabetes mellitus	Deaf-mutism
Muscular atrophy	Otosclerosis
Pigmentary degeneration of the retina (retinitis pigmentosa)	Osteosclerosis
Absence of lens	True dwarfism
Glaucoma	
Coloboma	
Displaced lens	
Paralytic drooping of eyelid	
Acholuric jaundice	

SEX-LINKED RECESSIVES.

Gower's muscular atrophy	Multiple sclerosis
Hemophilia	Coloboma
Color blindness (Daltonism)	*Microphthalmia*
Night blindness (nyctalopia)	Hereditary nystagmus
Neuritis optica progressiva	Hereditary toothlessness
Myopia	Ichthyosis

Questionable Dominants or Recessives.

Probable or suspected dominants.

Cystinuria
Gout
Defective hair and teeth, or teeth alone
Extra teeth
Hare-lip
Cryptorchidism
Hypospadias
Otosclerosis

Probable or suspected recessives.

Hereditary ataxia
Otosclerosis
Hereditary tremor
Cretinism
Splenic anemia
Stammering
Chlorosis

Undetermined Predispositions.

Cancer
Pneumonia (lobar)
Hernia
Spasmodic croup
Arthritis deformans
Scoliosis
Angioneurotic edema
Peptic ulcer
Gout
Allergic state
Pernicious anemia
Tuberculosis?
Diphtheria?

CHAPTER IV.

THE DEFENSE AGAINST INHERITED FACTORS.

The evidence of heredity is so strong in some diseases and abnormal states that they are already in the position of being attacked at their source through attempts to intercept or oppose their cause. The principles of prevention are clearly applicable in the defense against inherited factors. Hereditary disease is not inevitable in the human race for almost without exception, those in which the mode of transmission is known, can be prevented. In all probability innumerable cases of hereditary cataract, insanity, or hemophilia, to name but a few diseases, have been evaded for no other reason than the fact that chance mating and the number of offspring, worked against them. Conscious control should be able to do the same by selective mating, out-breeding and the control of progeny. Animal breeding has given valuable indications that these things can be done. Blanket measures are applicable against hereditary defects. The use of such measures is exemplified in the efforts to prevent a group of disorders of the nervous system which appear to be partly the result of an inherited instability of the nervous mechanisms.

A similar possibility exists against the allergic group of diseases in which the hypersensitiveness may not be specific to any one antigen but is a group specificity. It is possible that some errors of metabolism may fall in the same class. In each instance the preventive efforts against one condition may result in the prevention of many others.

The practising physician is constantly finding instances of family tendencies and he is therefore in a position to recognize and study these clinical phenomena. What he can do to prevent their propagation through faulty mating will depend on his influence among his patients' families as adviser as well as physician. This was a responsibility felt very heavily by the doctors of former generations, for they were interested in the family problems of their patients, rejoicing with them at births, and as deeply affected by engagements to marry as by the impending death of their patient-friends.

The part of confidential advisor can hardly be less the duty of the attending physician than the cure of disease. Although his advice may not be taken he should always warn, for there is no one so well informed on the hereditary diseases as he, and no one better placed to issue the warning.

The doctor's judgment and advice on the advisability of marriage must be made as far as possible on known or strongly supported facts as to the probabilities of harmful inheritance and a sound knowledge of how germ-plasm-borne diseases are transmitted. His advice as to whether two young people should marry, in both of whose families he is aware of a strong recessive harmful character, should be only as specific and as emphatic as the facts may warrant. On the other hand the presence of a harmful characteristic on one side of the union which may be suppressed by a satisfactory mating, need not imply that the persons involved should not marry. But such advice must be given with the understanding that at least the first and second filial generations must be considered: if the doctor's advice can ever be expected to be taken on such remote possibilities.

It should be possible therefore for the private practitioner to aid in the application of blanket measures against hereditary diseases for the good of the individual and the betterment of society. The appeal to family pride is often the strongest motive on which he can depend.

Blanket measures toward social and race improvement have been tried as long ago as the Spartans and as recently as the new eugenics movement started by Galton. All have failed or succeeded according to the applicability of the measures to the aims in view under the existing social order. Although the present discussion is limited to hereditary disease and is not primarily concerned with raising super-men whatever preventive measures may be used must be adapted to the customs of the times and place. What the private doctor might try to do for a few is assumed by some to be the function of the State for the many on the argument that since the education of the masses and the care of the helplessly constituted individuals is today an admitted function of the State, the prevention of the propagation of uneducable and socially unfit liabilities should also be the duty of the State. On principle, this can be accepted. The difficulty comes in knowing the liabilities; or, put in another way, can the possible hidden assets be ignored? Pearl[1] has expressed the dilemma by saying that the only guarantee of the worth of an individual for the breeding of a superior race is not his own superiority but the superiority of his progeny.

Hereditary cataract is a strong Mendelian dominant, albinism is a recessive, and hemophilia a sex-linked recessive. Can or should the State legislate against the marriage of persons showing these defects because their children may become wards of the State? It would undoubtedly be a blessing to a family to be purged of such impure members but what of other qualities of definite usefulness

[1] Pearl, Raymond The Biology of Superiority, Am. Mercury, November, 1927.

which they might possess and which would be lost in the same elimination process?

Feeblemindedness and hereditary insanity are defects of another order of liability in that the subjects of them are incapable of voluntary submission either to accepted social standards or legislation and are therefore of positive harm to future generations.

Between these extremes are all grades of undesirable hereditary traits which should be weeded out but there is always the fear of losing good grain with the weeds, or of transgressing personal liberties.

The methods now in vogue for the prevention of the obviously undesirable and insane are segregation, sterilization, and non-certification for marriage on physical or mental grounds. Efforts through birth control are found in almost every community but they flourish only so far as social tolerance permits them.

It would be beyond the scope of this work to review the opinions expressed on the merits and evils in all these measures, or to attempt to abstract the regulations for their practice. That there is much to be said to the advantage of each can hardly be doubted if strict adherence is to be given to the aim in view. Each will probably increase in popularity according to the circumstances under which it is urged, and preventive medicine can look with favor on any one which works and gains its ends so long as fanatic enthusiasm does not carry it beyond its bounds.

The physician in a community must be a potent force in creating sane attitudes towards social medical preventive measures. There can be little excuse for him to stand aside and take no part in the support of measures which he hopes will be effective in reducing hereditary disease. Every physician favors eugenics at heart, he has the knowledge of what is required to put his convictions into effect, and he will, in the future, add to his usefulness and his prestige if he does so.

As the problem of the prevention of hereditary defects narrows down to the particular failures in the genetic pattern of the individual the preventive measures to be applied will not be against the inheritance of the condition but against its development, for the individual is already a realized individual who has progressed to one, ten or sixty years of age under the influence of his environment within the limits set by his inheritance. The conditions with which the doctor is most concerned are not the congenital structural deformities and anomalies but the diseases which depend for their development on the operation of environmental causes in addition to the inherited factors. In them he is faced with the tantalizing thought that given an inherited trend (the idea of a gene as a determiner only, has here a special appeal), he may be able to assist the individual bearing it to adapt himself to his environment or

to control the environment in some way so that the disease may never develop.

Such hope is held out for the future control of diabetes mellitus, arteriosclerosis, cancer, gout, allergic asthma, hypersensitizations, otosclerosis, and other suspected but not definitely proven hereditary tendencies.

The Natural History of an inherited disease extends backward through the ancestry of the affected individual and is potentially repeated forward in his progeny. Unfortunately, the present understanding of many such diseases and disease tendencies does not permit the construction of the entire chain of events through which they progress. Nevertheless, the presence of vulnerable points in the natural histories of such as are known makes it possible to direct preventive activities against them. As has been pointed out heterozygous or homozygous characters can be prevented from coming together by regulation, sterilization, or intercepting the union of ova and sperm by any number of methods. Or once united into a defective zygote there are possibilities that certain agents can be used to counterbalance the faulty gene influence and that these can be consciously applied; for example, desensitization to foreign proteins in a hereditarily hypersensitive individual. Furthermore, known secondary causes which may enter the chain of events can be opposed or inhibited by the use of any available means, such as careful regulation of the diets and habits of potential diabetics and peptic ulcer cases.

Because the zygote is individual and unique, probably the greatest results in prevention will be obtained by methods which are individual in their application. It can hardly be expected that the social order will arrive at complete enough understanding to apply effective measures against most hereditary diseases, but there is every reason to believe that the physician in practice will some day attain enough knowledge and insight into the mechanisms of heredity to be able to advise, warn, guide and treat those of his patients with known inherited factors of disease to an extent that will materially reduce the number of defective and inefficient patients in his and subsequent generations.

CHAPTER V.

CATEGORY II: DEFECTS OF NUTRITIVE ELEMENTS.

THE NUTRITIVE ELEMENTS IN HEALTH AND DISEASE.

A FOOD is any substance which, when assimilated by an organism is useful in its growth, development and repair, or is of use in the normal processes of digestion: its main criterion is utility.

Distinction must be made between utility and utilization. A substance which is useful to the body may be prevented from being used by some alteration of function or structure of the alimentary tract. Thus certain enzymes necessary for the breaking down of complex protein molecules may be absent from the stomach or intestinal secretions, and therefore the native proteins will not be reduced to a condition in which they can be absorbed and used by the tissues. The protein is unchanged in its usefulness but it is not in a form which can be utilized. The importance of this distinction lies in the acceptance of utility as a criterion by which a substance is judged to be a food: it is the starting point in the discussion of the mechanisms of nutrition.

Usefulness implies the satisfaction of a need or requirement. A food, from this point of view is a substance which is needed by the body for the purposes mentioned in the definition, and conversely any ingested substances for which the body has no need is not a food but a contaminant of the food supply. Any material which cannot be absorbed from the gastro-intestinal tract and which is not useful in the performance of any function of the alimentary system is not a food; also, any substance which may be absorbed and carried to the body tissues but is not useful to any metabolic or vital processes, is not considered to be a food. In both of these examples there is no body requirement for the materials although they may pass through certain mechanisms capable of disposing of them. The fact that they may appear in body processes does not imply that they are needed, but on the contrary, may be positively harmful.

The food requirements of the body are determined by the total needs of its component parts. In the complex human organism all tissues and cells do not require equal amounts of the different nutritive elements because of specialization of function. Thus the red blood cells contain 80 per cent of all of the iron in the body and iodine is almost entirely utilized by the thyroid gland. A thorough understanding of the processes in which the individual food elements are involved is as essential as the knowledge of their chemical and biologic qualities and quantitative requirements.

Food is essential for the maintenance of the balanced mechanisms of the body through all stages of growth and development. These mechanisms have been built up from the beginning of ontogeny by the continued differentiation of parts and the constant assimilation of food. Provision is made for the elimination of waste and the disposition of unnecessary or harmful substances and a balance is thereby assured between the nutrient supplied and the relatively stable equilibrium of the organism.

CLASSIFICATION OF FOODS.

The majority of foods are not in a form for immediate use by tissue cells and must be prepared by the processes of digestion. This preparation is of the nature of reduction of complex compounds and the breaking up of the physical structure of raw food particles.

Although food is generally thought of as the raw and cooked materials which are eaten as such, there is another conception that considers it not in its bulk, but in the smaller chemical elements of which it is composed. But even these are still further divisible into the final forms which can be utilized immediately by the body.

The raw bulky state, in most instances is too crude and complicated to permit detailed knowledge of its usefulness. A piece of beef steak for example cannot be studied as a steak but must first be analyzed and investigated in its physical and chemical units.

Nor can the problem of nutrition be approached only from a study of the final forms to which food can be reduced by physiologic processes. To investigate the amino-acids and monosaccharides as they are absorbed from the gastro-intestinal tract would give little information as to the preceding states of these materials with which the body has to deal.

It is desirable to know what are the fundamental physical, chemical and biologically active units of which the food supply is composed in its native state and before it has been acted upon by digestive and assimilative processes.

Chemical and biologic analysis of foodstuffs has revealed relatively few primary classes of food elements. More are certain to be added in the sub-classes into which they can be divided but there is little indication that the number of large groups themselves will be increased.

The present knowledge of nutrition recognizes the following classes of food principles, food elements, nutritive elements or nutrients as they are variously called:

I. Water	IV. Fats
II. Proteins	V. Inorganic salts and minerals
III. Carbohydrates	VI. Vitamins

Since these are the fundamental unit forms in which food is supplied to the body they have been selected as the basic elements of a categorical group capable of causing disease by defects in their supply or utilization. They are all potentially useful and each fulfills a need.

In order to comprehend more fully the effects of deficiency or excess of the nutritive elements it will be necessary to review the mechanisms through which they exhibit their usefulness and the functions and processes dependent on them.

FOOD REQUIREMENTS OF PROTOPLASM.

The primary needs of protoplasm are materials which it can synthesize and assimilate or bring into association with itself, and energies necessary for its vital processes. Since protoplasm is constantly utilizing these materials and performing work it is an exhaustible mechanism and the food and energy requirements must be resupplied. Protoplasm can not therefore be self-sustaining but must depend for its food-energy source on its environment.

All protoplasm so far analyzed is dead protoplasm, and although it can be said that C.H.N.O. and S. are constantly present this is far from stating its actual composition. Organization seems to be the greater part of the explanation of protoplasm for it is possible to synthesize *in vitro* many compounds of C.H.N.O. and S. but they do not make protoplasm. Other elements found less constantly in allegedly pure protoplasm analyses may be just as important to the living substance as those listed above and to consider them as unessential or contaminations begs the question for in many instances it is found that the full expression of the protoplasmic activity is impossible without them.

Plant and animal physiology differ in their nutritive processes largely in the form of the nutritive elements which they can utilize. Plants can synthesize proteids from simple chemical elements but animals cannot and animal life is possible only as a form of parasitism on plants. Since the present concern is only with the physiology of animal nutrition all references to protoplasm and tissue needs will be understood to apply to animal organization.

CHAPTER VI.

THE NUTRITIVE ELEMENTS IN HEALTH AND DISEASE.

WATER.

WATER is the most important material need of protoplasm and makes up from 60 to 85 per cent of its bulk. In the human body water accounts for approximately 70 per cent of the weight. The water content of a man of average size is about 100 pounds.

This fluid volume is present in three main states; the circulating fluids in the blood and lymph channels, the relatively static "bog" of liquid in tissue spaces and between the cells, and the intracellular fluid component of protoplasm.

The functions of water require that it be constantly in motion. That which is spoken of as circulating is only relatively more in motion than that which has "inundated" (Cannon's term) the tissue spaces and this last is only comparatively actively moving in contrast to the water within the cells. Every molecule of water which the body has assimilated from its environment eventually passes through these three states.

At various points on this circuit the water becomes lost to the body by virtue of its participation in eliminative processes to which it is essential. Thus, the water which passes through the capillary tufts of the renal glomeruli becomes involved in the elimination of waste products and the formation of urine; that which reaches the tissues lining the alveoli of the lungs and mucous membranes is lost directly from these surfaces; external secretions such as tears, milk and sweat carry off several pounds of water per day to the external environment.

All of this fluid loss must be replaced. Although the internal water circuit may be maintained for a time by the continuation of metabolic processes this very activity itself promotes further loss. Although there are defense mechanisms which operate to conserve the fluid matrix they are incapable of maintaining the water balance unless more can be obtained from the environment. *Life itself* is dependent therefore on the consumption of water.

Water is the medium in which all physiologic processes take place. It is the mother liquor that makes possible the solution of electrolytes, the passage of materials through cell membranes, the transportation of particulate matter, such as blood cells, and chemical ingredients like hormones, enzymes, amino-acids and acid-base

substances. Water acts as a mechanical protection against physical injury by lubricating serous surfaces and by interposing itself as cerebrospinal fluid between the sensitive nerve tissues and their unyielding containers. The maintenance of body temperature depends to a great extent on heat lost and conserved through the control of water evaporation from external surfaces.

Although a considerable amount of the water supplied to the body is in the form of bound water in the so-called solid foods, this source is inadequate and is supplemented by the consumption of various drinks and beverages. The manner and amount so consumed is largely conditioned by the time of meals, taste, drinking habits, and the use of various food adjuncts such as gravies and sauces. Most people also demand the cooling effect of water taken by itself in varying amounts throughout the day. Individual habits of drinking are largely regulated by the mechanism of thirst. Cannon has shown that thirst is a physiologic response to fluid demand manifested by local dryness of the throat which becomes uncomfortable until the demand be met. Thirst may be looked upon as a need produced by an imbalance in a regulatory mechanism which makes use of conscious effort for its satisfaction.

Daily Fluid Intake.—Only recently has a clear understanding been obtained of how much water should be consumed in a day. The newer knowledge of water metabolism emphasizes the flexibility of water reserves, especially in the skin and muscles. These reservoirs and others are constantly giving up and receiving water in response to activities in other tissues and, within the limits of physiologic equilibrium, are well able to take care of all ordinary requirements. It is not necessary to consume large amounts of water in order to "flush the kidneys," give fluid to the fecal contents, increase the milk supply, and to perform many other idealistic feats of physiology. These functions do not depend on the volume of water supply alone and are little affected by it without the intervention of other physiologic factors.

What is required is a maintenance of water balance in general so that when individuals are advised as to how much water and beverages they should consume consideration should be given the fact that the supply from such sources need only be supplemental to the water content of the twenty-four-hour food intake. The average daily intake of water or other fluids for an adult should be 2 to 4 liters (4 to 8 pints).

It is interesting to note the water content of some of the common so-called solid foods:

Beef loin, 60 per cent; tongue, 70 per cent; liver, 71 per cent; roast, 48 per cent; ham, 40 per cent; bacon, 18 per cent; bologna sausage, 60 per cent; chicken, 75 per cent; fish, 60 to 80 per cent; oysters, 86 per cent; boiled egg, 73 per cent; cheese, 34 per cent;

butter, 11 per cent; boiled rice, 92 per cent; wheat breakfast foods (average), 9.6 per cent; breads (average), 35 to 40 per cent; toast, 24 per cent; soda biscuit, 23 per cent; lima beans, 68 per cent; asparagus, 94 per cent; string-beans, fresh, 89 per cent; string-beans, cooked, 75 per cent; carrots, 88 per cent; cauliflower, 92 per cent; celery, 99 per cent; lettuce, 94 per cent; potatoes, 78 per cent; spinach, 89 per cent; apple, 89 per cent; orange, 87 per cent; strawberries, 90 per cent; almonds, 5 per cent; peanuts, 10 per cent.

In a sample diet taken at random from a book on dietetics the total amount of "solid foods" to be taken in one day was 1355 grams. Of this amount 1023 grams was water.

Water Starvation.—As long as one is not actually starving, fluid loss is being made up in part by water in the solid foods. But unless this be supplemented by beverages and other forms of liquids, the drain on the tissue fluids may lead to serious derangements of metabolism. The ordinary physiologic checks against imbalance of water distribution, such as the regulation of the salt and protein content of plasma and lymph, the maintenance of an acid-base equilibrium, effective thyroid activity, efficient blood-pressure and kidney glomeruli inter-relationships, and satisfactory glandular activities in general, cannot operate effectively for long on an inadequate fluid supply which forces them to call continuously on tissue reserves. As a result of this repeated borrowing of water from some tissues and paying back only in part by others a serious shortage eventually occurs in vital organs, and death ensues. The limit of tolerance however is great as can be attested by the many persons who have experienced serious water starvation following shipwreck and other disasters but who were rescued and restored to health. Under less dramatic circumstances there may be no more serious disturbances than thirst, muscular cramps, abdominal pain, weakness, and the typical "fallen in" appearance of the dehydrated person. These can be overcome very quickly by drinking water or the administration of liquids by artificial means. In the healthy, such temporary deprivation produces no permanent damage to any organ or causes any irreparable alteration of vital functions.

Prolonged inadequacy of liquids, short of serious water starvation, may eventuate in disturbances of other mechanisms which depend on water. This is especially true of nitrogen metabolism as evidenced by an increase in blood and urine urea under these conditions. Van Slyke[1] is of the opinion that this is not due to impaired excretion but is the result of augmentation of nitrogen catabolism. Long-continued deficiency of water results also in increased concentration of blood hemoglobin, plasma and serum protein, and diminished blood volume.

[1] Peters, J. P., and Van Slyke, D. D.. Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1931.

When the fluid intake is lessened, not by voluntary starvation or an inadequate supply of water, but by morbid conditions, such as coma, acidosis, vomiting, poisoning and various intoxications and by any diseases altering the utilization of water, or diseases in which fluid loss out-balances the supply, the consequences are far more marked. Maintenance of water balance is imperative under these conditions and clinical custom has long dictated the need of forcing fluids in their treatment.

Water Intoxication.—Excesses of fluid intake are ordinarily handled satisfactorily by the excretory mechanisms. It requires exceptional amounts of water to produce any detectable blood volume increase or serum or plasma protein decrease. If the urinary output is diminished by disease or the action of drugs such as pituitrin, a condition of "water intoxication" may be brought about. This is characterized by headache, nausea, dizziness, weakness and *incoördinated movements. In animal experimentation it has produced* convulsions. A similar syndrome results when water has been taken too freely by those who have just done a turn at work under hot dry conditions where they have been temporarily unable to quench their thirst.

Water with Meals.—Besides the total amount of water consumed per day and its physiologic function in maintaining water balance some attention must be given to the manner in which it is taken; that is, to the part which it plays in a process as distinct from its nutritive nature.

Reference has already been made to the response to thirst. This should be the main guide to the consumption of water and beverages *both during and between meals. It is not only unnecessary but may* be harmful to drink large volumes of liquids between meals simply through habit or in response to fads.

At meal-time, the consumption of anything but a moderate amount of water is a pernicious habit because it is indulged in not for the satisfaction of thirst but for other non-physiologic purposes. The thirst should have been satisfied before coming to the meal, whether it be by the early glass of water before breakfast or the light drinks during the later morning or afternoon. To see a person drench himself with large glasses of water at meals is to witness a physiologic insult; the water consumed is far beyond what is needed to satisfy the thirst and is usually taken to wash down poorly masticated food. The excess water disturbs the secretory activity of the stomach, especially if it is ice water; it dilutes the gastric secretions, and if taken at the beginning of the meal may alter considerably the emptying time of the stomach. In general it seems best that thirst should be satisfied before coming to the meal, and that only a moderate amount of water be taken during

the middle and latter courses of the meal, if at all, and even then not too cold. Never use water to wash down food.

Water enters into many processes that act as contributing causes of disease: as a vehicle for substances dissolved or suspended in it, water becomes an important factor in the natural history of a large number of intoxications and in all of the water-borne diseases; its physical qualities make it important in the heat regulation of the body; its presence in overwhelming amounts in the lungs results in drowning. The discovery of heavy water is of profound interest to the physiologist and bio-chemist and may eventually demand the serious consideration of the pathologist.

The rôle of water in many other mechanisms and processes is discussed in subsequent categories.

CHAPTER VII.

THE NUTRITIVE ELEMENTS IN HEALTH AND DISEASE (CONTINUED).

PROTEINS.

PROTOPLASM is largely made up of proteins; proteins are combinations of amino-acids; amino-acids are synthetic products of carbon, hydrogen, nitrogen, oxygen, and often sulphur and phosphorus. Man is physiologically incapable of synthesizing proteins or amino-acids from the native elements. But given amino-acids in his diet he can, by combining them in various ways, make protein and therefore protoplasm.

The variation in the qualities of different proteins is accounted for by the number and types of amino-acids of which they are composed. The tissues of the body vary in their requirements of the eighteen or twenty known amino-acids and in order that this selectiveness may be possible, the simple and conjugated proteins of the diet are hydrolyzed in the process of digestion into proteoses, peptones, polypeptides and the amino-acids. The latter are assimilable, that is they can be absorbed by the intestinal mucosa, carried into the tissues and combined to make the specific forms necessary for each tissue requirement.

The following table presents the list of digestive enzymes which act upon proteins, the tissues and secretions where they are formed and the stages of hydrolysis which they produce. A list of the known amino-acids is appended.

HYDROLYSIS OF PROTEINS.

Enzyme:	*Formed in:*	*Acts upon:*	*Hydrolyzes to:*
Pepsin	Stomach	Proteins	Proteoses Peptones Peptids Few amino-acids
Rennin	Stomach Pancreas	Casein	Peptone Paracasein
Trypsin	Pancreas	Proteoses Peptones	Amino-acids
Erepsin	Small intestine	Proteoses Peptones	Amino-acids

Amino-acids.

Glycocoll (glycine)	Tryptophane	Lysine
Alanine	Histidine	Aspartic acid
Serine	Valine	Glutamic acid
Phenylalanine	Arginine	Proline
Tyrosine	Leucine	Oxyproline
Cystine	Isoleucine	Norleucine

Assimilation of Proteins.—The reduction of proteins also converts them from the non-absorbable colloid state to the crystalloid amino-acids which can penetrate semi-permeable membranes. It is a moot question whether the resynthesis of the proteins takes place within or outside of the capillary circulation. If without, it must occur in places where the permeability of the capillaries will permit their passage through it and the only places in which this now seems possible are the liver, blood-forming organs, spleen and intestinal mucosa.

Some amino-acids pass through the liver and enter the general circulation of the body unchanged and remain unconjugated until they are brought into contact with tissue cells. The importance of knowing where resynthesis takes place lies in the fact that the colloid state of the proteins has an important bearing on the osmotic pressures within the capillaries and tissue spaces.

To satisfy tissue needs the protein intake must contain all, or at least all of the most important, amino-acids. It is not essential that each protein possess every known amino-acid (when it does it is called a complete protein) but that all essential amino-acids be represented among them.

Daily Protein Requirement.—The total daily protein requirement for man ranges from 1 to 1½ grams per kilogram body weight. This amount varies more with age than with activity because the main use of protein is as a tissue builder. In the younger age periods growth and development demand more of these tissue building blocks than is required by those past the growing stage who only need to replace destroyed tissues. Selectivity goes on however throughout life because all tissues need replacement. Therefore there is a continued need for a balanced, qualitative protein diet.

The caloric value of protein is 4.1 Calories per gram.

This energy in the protein molecule is due in part to its carbohydrate moiety which amounts to 58 per cent of its weight and becomes available when the molecule is broken down. (It is for this reason that the total glucose determination in a diet must take into consideration 58 per cent by weight of the protein intake.)

When protein enters into the processes of metabolism it not only supplies energy at the above rate but also stimulates tissue metabolism and thereby creates a greater demand for energy. Unless this energy is supplied the demand becomes greater than the supply and the tissue suffers from a loss which is estimated to be 30 per cent greater than the energy brought into the process by the protein. This stimulating effect is termed the specific dynamic action of protein. It is evident therefore that a purely protein diet could never supply itself with enough energy to maintain tissue metabolism. This may be expressed by saying "the more protein consumed, the more need to the consumer." Such a procedure could never

reach a state of equilibrium. There is at present no satisfactory explanation of this phenomenon and the specific dynamic action of protein remains an empiric observation.

Qualities of Proteins.—In discussing the amino-acid content of proteins the complete protein was said to be one which possessed all of the amino-acids. An incomplete protein may possess relatively *few* of the essential amino-acids and will therefore have less value as a tissue builder. Numerical values have been given to the common protein foods according to the positions which they occupy in a relative scale based on the value of their contained proteins. This numerical position is called the Biologic Protein Value (B.P.V.) of the food.

Biologic Values of Different Proteins, as Measured by the Percentage Quantity of Body Protein Which Their Ingestion will Spare from Loss (Thomas.)*

Ox meat	104	Yeast	71
Cows' milk	100	Casein	70
Fish	95	Nutrose	69
Rice	88	Spinach	64
Cauliflower	84	Peas	56
Crab meat	79	Wheat flour	40
Potatoes	79	Cornmeal	30
Cherry-juice	79		

* Thomas, K. Arch. f. d. ges. Physiol., 219, 1909. Julius Springer, Berlin.

Metabolism of Proteins.—The processes of protein metabolism after absorption are those of selective synthesis by tissue cells and the breakdown of tissue proteins into simpler nitrogenous and non-nitrogenous waste products. Between the time of their absorption as amino-acids and elimination as end-products lies a complicated cycle of resynthesis and proteolysis. The intermediate products are alternately utilized in the metabolism of tissues and cells and liberated by tissue activity. They may pass back and forth in this way many times before they are eventually excreted as end-products. This reutilization of intermediate products continues as long as protein is presented to the body in the form of food (exogenous protein), or in the absence of food, as long as the body proteins (endogenous proteins) can be called upon without endangering the nitrogen balance beyond recovery.

The first stage of intermediate protein metabolism probably occurs in the liver where the greater part of the proteins are deaminized, that is *are separated into their nitrogenous and non-nitrogenous* parts. From the former the plasma proteins, albumin, globulin and fibrinogen are formed by resynthesis; from the latter are obtained the carbohydrate and fatty acid moities (58 per cent and 46 per cent by weight of the protein molecule respectively). Other *non-protein nitrogenous intermediate products are also formed,*

such as urea, uric acid, creatinine and an undetermined nitrogen component called "rest-nitrogen." For the sake of visualizing the subsequent processes they may be considered as taking place "beyond the liver," that is, in the blood plasma, tissue fluids and cells. Analysis of the protein changes in these locations reveals that they and their intermediate products are in a continual state of flux but one which maintains an essentially relative equilibrium between its parts at all times. The serum proteins, the amino-acids which escaped deamination in the liver and those which have been formed by proteolysis of tissues, the carbohydrate and fatty acid moieties, the entire protein-nitrogen and non-protein nitrogen complex, are bound together in the physico-chemical processes of osmotic pressure, nitrogen balance, acid-base equilibrium and intracellular metabolism. Upon the maintenance of this balance-in-flux, depends not only existence itself, but protection against a wide range of pathologic-physiologic disturbances from those of serious import down to minor functional imbalances in its lesser processes.

Since the body requires a resupply of exogenous protein for its continued existence and since this supply may vary quantitatively and qualitatively with the food, there must be constant adaptation of the mechanisms of protein metabolism to this supply. Because the supply of protein may be defective and so lead to disorders of metabolism, this nutritive element may act as a categorical cause of disease.

Deficient Protein Intake.—There are a number of disease processes where a defective protein intake is involved. In infancy simple starvation readily results in a serious protein deficiency. This is especially true when the carbohydrate is low because of the "protein saving" quality of the carbohydrates. It has already shown how the proteins, through their specific dynamic action stimulate metabolism. Carbohydrates through their supply of energy conserve the energizing values of the proteins and permit them to fulfil their rôle as tissue builders. In the presence of a disturbed protein supply, or a relative disproportion between carbohydrates and protein intake when the latter is low, rapid wasting takes place with loss of weight, inanition and edema, the latter resulting from deficient colloidal plasma proteins to hold the fluids in the blood-vessels. The same processes are concerned in the nutritional edemas seen in famine areas and among people of excessively low economic social status. Under all of these starvation conditions the nitrogen balance cannot be maintained.

Although the exact etiologic factors in pellagra are not known there is strong evidence that it is caused by a defective supply of one or more nutritional elements. Of the various theories of its origin that of a dietary deficiency has been most widely accepted. Whether or not it is due to a qualitative or quantitative protein

defect, a vitamin, or an imbalance between several food elements must await further investigation. Although casein, a complete protein does not completely prevent the disease under experimental conditions, it modifies the appearance of the disease considerably. None of the known vitamins prevent it. Yeast in sufficient quantities will completely control its appearance but yeast is a complex substance containing proteins, vitamins and a possible further factor designated by Goldberger as the P.P. factor. This latter has not been isolated or demonstrated independent of the other factors. The nearest approach, at present, to an explanation of pellagra is that it is due to a deficiency of some factor or factors closely associated with the proteins.

Excessive Protein Intake.—An excess of protein intake in man appears to have no other effect than to increase nitrogenous elimination. This applies only to those whose nitrogen metabolism mechanisms are in normal equilibrium. The protective processes against permanent damage to the balanced state are apparently sufficient to care for all excesses which can be placed upon it. Of great interest is the alleged storage of protein in the liver in much the same way that this organ stores carbohydrate as glycogen. This storage power is suggested by changes in the microscopic appearance and protein content of the liver cells of experimental animals which had been starved and subsequently fed on proteins. Experiments on humans in which protein intake and output have been carefully measured present evidence of the same possibility.

There are many disease processes involving the intermediary phases of protein metabolism which are directly or indirectly affected by the quantity and quality of proteins supplied.

Gout has been long believed to have some relationship to the consumption of large amounts of food especially rich in purin bodies. It is not now believed that this diet *per se* is capable of producing gout but the gout is precipitated or aggravated by an abundance of purin products. Where the primary fault lies is not entirely known but present evidence points toward the inability of the kidney to handle the uric acid and other products of protein metabolism.

The thyroid is considered to exert some control over the storage of protein. Myxedema is believed to be one of the evidences of this. There is doubt that the thyroid is alone responsible for the mobilization of proteins on demand but that the adrenals and autonomic nervous system also participate in this function.

It has long been empiric practice to give low-protein diets in nephritis. This is probably because proteins are involved in several of the deranged mechanisms of renal disease. The protein diet becomes important only in so far as some one or more of these mechanisms is at fault and produce such symptoms as edema and

CHAPTER VIII.

THE NUTRITIVE ELEMENTS IN HEALTH AND DISEASE (CONTINUED).

CARBOHYDRATES.

THE carbohydrates are combinations of carbon, hydrogen and oxygen in which the hydrogen and oxygen are, with few exceptions, in the proportion to form water (H_2O). Their general formula is $C_nH_{2n}O_n$.

They are found in the dietary of man as the sugars and starches of his vegetables, fruits, berries, milk and dairy products, honey, cereals, breadstuffs, nuts, and an available portion of the proteins and fats of animal and vegetable foods. Their widespread occurrence makes them unavoidable even in the most bizarre diets of natives who apparently restrict themselves entirely to meats and fats.

Aside from the carbohydrate moiety of proteins and fats the bulk of the carbohydrate intake is in the form of the polysaccharids and disaccharids, that is, in combinations of two or more molecules of the monosaccharids or simple sugars.

Assimilation of Carbohydrates.—The assimilation of the carbohydrates necessitates that they be in solution in the digestive juices in a form that can pass through the semi-permeable membrane lining the digestive tract. The polysaccharids are either insoluble in aqueous solution or are in the form of colloids and therefore cannot be absorbed as such and the disaccharid molecule is too large for dialysis through the epithelial membrane.

Since few of the carbohydrates of the diet are presented in the form of simple sugars (monosaccharids) there must be some mechanism provided to reduce the poly- and disaccharids to an assimilable form. This is accomplished by their hydrolysis under the action of the digestive enzymes secreted by the salivary, gastric, pancreatic and intestinal glands.

The common representatives of these classes of sugars are:

I. *Monosaccharids:*
   - Glucose or dextrose (grape sugar).
   - Galactose (constituent of milk sugar).
   - Levulose or fructose (fruit sugar).

II. *Disaccharids:*
   - Maltose (malt sugar).
   - Lactose (milk sugar).
   - Sucrose or saccharose (cane sugar).

III. *Polysaccharids:*
   - Starch.
   - Dextrin.
   - Glycogen.

In the hydrolysis of the disaccharids, maltose produces two molecules of glucose; lactose breaks up into one molecule of glucose and one of galactose; sucrose yields one molecule of glucose and one of levulose. These end-products are soluble and dialyzable.

The hydrolysis of the polysaccharids is more complex in that they require the formation of intermediate products before they are entirely reduced to monosaccharids.

They are converted by salivary and intestinal enzymes through the following stages:

HYDROLYSIS OF CARBOHYDRATES.

- Starch
  - Maltose
    - Glucose
    - Glucose
  - Erythrodextrin
    - Maltose
      - Glucose
      - Glucose
    - Achroodextrin
      - Maltose
        - Glucose
        - Glucose
      - Maltose
        - Glucose
        - Glucose
- Dextrin
  - Erythrodextrin
    - Maltose
      - Glucose
      - Glucose
    - Achroödextrin
      - Maltose
        - Glucose
        - Glucose
      - Maltose
        - Glucose
        - Glucose
  - Achroödextrin
    - Maltose
      - Glucose
      - Glucose
    - Maltose
      - Glucose
      - Glucose

Digestion of Carbohydrates.—The enzymes which hydrolyze the *carbohydrates are listed below, with the tissues and secretions in* which they are found and the end-products of their activity on their selective carbohydrates:

Enzyme:	*Formed by:*	*Acts upon:*	*Hydrolyzes to:*
Ptyalin (Salivary diastase)	Salivary gland	Starch	Maltose
Amylase (Pancreatic diastase)	Pancreas	Starch Dextrin Glycogen	Maltose
Invertase	Small intestine	Sucrose	Glucose Levulose
Maltase	Small intestine and Pancreas	Maltose	Glucose
Lactase	Small intestine	Lactose	Glucose Galactose

Daily Requirement of Carbohydrates.—The total carbohydrate requirement of the body is generally expressed in terms of glucose. Since proteins yield an amount of carbohydrate known as their carbohydrate moiety this must be included in the total. Fats also yield an available supply. Woodyatt expresses the total glucose content of a diet by the following formula:

$$\text{Glucose} = \text{Carbohydrate} + 0.58\ \text{Protein} + 0.10\ \text{Fat}$$
$$(G = C + 0.58\ P. + 0.10\ F.)$$

Carbohydrates serve their greatest purpose to the body as sources of energy, burning with a caloric yield of 4.1 calories per gram. If the supply of carbohydrates in the diet is withdrawn, those stored in the tissues and the available carbohydrate in the proteins and fats of the diet and body tissues are called upon to supply more energy. Such borrowing cannot continue for long and the mechanisms of carbohydrate storage and use soon break down. Because the carbohydrate requirement varies greatly with the caloric demands of the entire body the amount needed daily cannot be indicated in any definite number of grams per kilogram body weight as with the proteins.

Bodily activity and the amount of fat and protein in the diet are the important determiners of how much carbohydrate is needed. Basal requirements call for about 30 calories per kilogram of body weight but this may be doubled under conditions of continued activity. The nearest approach to an average consumption of carbohydrate in an average adult diet would be between 400 and 500 grams.

Many factors enter to raise the total caloric requirement above the basal level. These are: age, sex, amount of work to be done, weight, state of nutrition, and climate. The carbohydrate intake will vary therefore with the caloric demands due to these factors.

Sources of Carbohydrates.—The carbohydrate content of most foods has been determined. The following partial list from Joslin[1] shows the vegetables arranged in tabular form according to per cent of carbohydrates:

VEGETABLES (FRESH OR CANNED).

1–5 per cent.		*10 per cent*	*15 per cent.*	*20 per cent.*
Lettuce	Tomatoes	Onions	Green peas	Potatoes
Spinach	Rhubarb	Squash	Artichokes	Shell beans
Sauerkraut	Eggplant	Turnips	Parsnips	Baked beans
String-beans	Leeks	Carrots	Lima beans	Green corn
(very young)	Beet greens	Okra	(very young)	Boiled rice
Celery	Watercress	Beets		Boiled macaroni
Asparagus	Cabbage	String-beans		Lima beans
Cucumbers	Radishes	Brussels sprouts		
Sorrel	Kohl-rabi	Pumpkin		
Endive	Broccoli			
Dandelions	Vegetable			
Swiss chard	marrow			
Sea kale	Mushrooms			
Cauliflower				

[1] Joslin, Elliott P.: Treatment of Diabetes Mellitus, 6th ed., Philadelphia, Lea & Febiger, 1937

Carbohydrate Content of Fruits and Nuts (Compiled From Various Sources).

Fruits.

1-5 per cent.	5-10 per cent.	10-15 per cent.	20 per cent.
Ripe olives	Lemons	Apples	Plums
Grapefruit	Oranges	Pears	Bananas
	Cranberries	Apricots	
	Strawberries	Blueberries	
	Blackberries	Cherries	
	Gooseberries	Currants	
	Peaches	Raspberries	
	Pineapple	Huckleberries	
	Watermelon		

Nuts.

1-5 per cent.	5-10 per cent.	10-15 per cent.	20 per cent. +
Butternuts	Brazil nuts	Almonds	Peanuts
Pignolias	Black walnuts	English walnuts	Chestnuts (40 per cent)
	Hickory	Beechnuts	
	Filberts	Pistachios	
		Pinenuts	
		Pecans	

Generalizations on Other Foods

Shellfish—all less than 5 per cent
Fish—all less than 5 per cent.
Meats—all negligible.
Dairy products—all 5 per cent or less
Cream average, 3 0 per cent, whole milk, 5 per cent, skimmed milk, 5 1 per cent.

The great variability in the caloric requirements makes it unnecessary to figure any closer than 5 per cent limits in practical dietetics. Accurate determinations for metabolic studies and experimental investigation will necessitate reference to original food analysis tables.

In refined calculations further consideration must be given to the availability of the ingested carbohydrates because all natural forms of sugars and starches cannot be prepared by the digestive processes for complete assimilation. The amount of cellulose in the whole food, the compactness of the small laminated starch granules, the water content, and the presence of pectin interfere with the proper break-up of the food in the digestive tract and the ease with which the enzymes, acids and alkalies of the digestive juices can attack the smaller food particles. Although boiling and cooking softens the food and in some instances carries the starches through the first processes of hydrolysis it never completely changes the entire food to a digestible form. There is always left an insoluble or undigestible residue which is eliminated in the feces. In general it may be said that 3 per cent of the 5 per cent vegetables and 6 per cent of the 10 per cent vegetables is available.

Sugars (and starches when they have been reduced to sugars) may undergo fermentation before they can be absorbed. This

generally takes place under conditions that will not permit them to be *assimilated, in the time allotted for the amount involved*, in their passage through the stomach and intestines. A large bulky carbohydrate meal may pass beyond the action of the digestive juices before they have had time to act on it; a smaller amount *may be delayed in the stomach* and there undergo fermentation before it has reached the absorbing membranes of the intestine.

The preceding discussion has presented briefly the qualities and characteristics of the carbohydrates as they are presented to the body for utilization. Further consideration of the processes which may interfere with their utilization will be given in the later chapters.

Metabolism of Carbohydrates.—After absorption, the three monosaccharid sugars, glucose, levulose and galactose enter almost immediately into the processes of metabolism. Glucose is by far the most important of the three for it is believed that levulose and galactose are converted into glucose on reaching the liver.

In the liver, glucose partakes in the first energy exchange when *it is converted into glycogen. The process by which glucose is* changed into liver glycogen (animal starch) is called hepatic glycogenesis and is brought about by specific tissue enzymes. The main function served by this conversion is carbohydrate storage, from which glucose can be obtained as needed. The glycogen is stored within the hepatic cells and the total amount which they can accommodate is between 150 and 200 grams.

A small amount of the circulating glucose in the portal radicles is probably used directly by the liver cells. This is accomplished by enzyme action which transforms the glucose (glycolysis) into lactic acid, CO_2 and water.

When the body requires carbohydrate, a reversal of the process of glycogenesis occurs (hepatic glycogenolysis) in which the glycogen stored in the liver is converted again into glucose and discharged into the arterial circulation.

Up to this point most of the absorbed glucose has been utilized by the liver either by conversion into glycogen or combustion by the hepatic cells. A small amount does not become involved in these processes but remains in the circulation and is carried through the liver. This original absorbed glucose in the circulation is joined by whatever glucose has been formed from liver glycogen. These mixed glucoses are then carried to the body tissues.

In the tissues the glucose brought from the liver (hepatic glucose) is *again converted into glycogen* (tissue glycogenesis). This secondary storage is most pronounced in the muscles.

A second glycogenolysis takes place in the tissues (tissue glycogenolysis) by which the tissue glycogen is reconverted into glucose and becomes available, by reduction (tissue glycolysis) for tissue use. This roundabout use of the hepatic glucose seems to be neces-

sary because of some peculiar property which it possesses which does not permit it to be used directly from the blood.

It has been stated above that glycogenolysis occurs as carbohydrate is needed. The controlling mechanisms of carbohydrate metabolism rest on this fact; *i. e.*, the storage and liberation of carbohydrates in the liver and tissues is regulated in response to physicochemical demands that are in turn dependent upon the carbohydrate supplies of the body. The nature of this mechanism is evident but the full explanation of its processes is not yet possible.

Insulin.—Before discussing what is known of the adjustments by which carbohydrate equilibrium is maintained attention must be drawn to the rôle of insulin, the internal secretion of the islets of Langerhans of the pancreas.

Insulin acts primarily by inaugurating the conversion of circulating hepatic glucose into tissue glycogen (tissue glycogenesis). It is also probable that it is instrumental in hepatic glycogenesis.

In the normal subject the stimulus to the secretion of insulin seems to be a high blood-sugar level. It is believed that hyperglycemia stimulates the islands of Langerhans directly to produce more insulin, but there is also evidence that there is some nerve stimulation through the vagi. Cannon does not believe that this latter is necessary but at the same time does not imply that it is useless.

The operation of the mechanisms of blood-sugar level maintenance can be followed best by studying the effects of a heavy carbohydrate meal.

In the normal individual, ingestion of 500 grams of glucose results in the rapid absorption of this readily available monosaccharid and its transportation by the portal circulation to the liver. In the liver glycogenesis takes place immediately but this process cannot keep pace with the demands and the excess overflows into the arterial circulation and is carried around the body. Cannon believes that a considerable quantity of such glucose is deposited in the skin without undergoing chemical change. The first measurable result of this flooding of the arterial blood is to raise the blood-sugar level. This normally ranges between 0.09 and 0.120 milligrams per 100 cc. of blood. Under sudden carbohydrate excess it rises to 0.160 or 0.170 mg. per cent which constitutes hyperglycemia. The hyperglycemic blood now apparently stimulates insulin production and this hormone in increasing amounts in the blood causes the circulating glucose to be converted into tissue glycogen. This means sugar loss from the blood and a consequent lowering of the blood-sugar level. At the same time circulating blood sugar is carried through the liver where hepatic glycogenesis causes further reduction of the blood-sugar level. Muscle activity and other tissue needs consume the tissue glycogen and this loss restores the

carbohydrate balance to *normal and the blood-sugar level to its* normal range.

Effects of Disturbed Carbohydrate Utilization.—Fasting results in very little measurable change in blood-sugar level because lack of carbohydrate coming from the intestine is made up by the release *of glycogen stored in the liver and muscle.* As long as the use of these reserves continues the body can also call upon the proteins and fats for their share of carbohydrate-forming elements. Each of these processes is competent to maintain the blood-sugar level for a limited period of time. The factor that determines the final *breakdown of this mechanism is depletion of the glycogen reserve* and the harmful effects of deranged protein and fat metabolism.

Fat is synthesized in the body by conversion from the carbohydrates and the combustion of fat is dependent upon the oxidation of sugar. This is given common expression in the saying, "The fats burn in the fire of the carbohydrates."

If the carbohydrate supply in the diet is inadequate or not utilized the call upon the fats and proteins for their carbohydrate content exhausts these available energy resources of the body. Incomplete combustion of the fats then occurs with the formation of poisonous β-oxybutyric and aceto-acetic acids; the acids of acidosis.

The carbohydrate mechanism operates continuously in the body economy. It participates in the balances between the cellular components and their complicated internal and external environments, and it is manifested in the reactions between cells, tissues and organs *far separated from each other throughout the body. Many laboratory* and clinical procedures reveal cross-sections of these events and from them interpretations are made of what is taking place at the point of investigation and an understanding of the normal and abnormal processes of carbohydrate metabolism is gained by piec*ing them together.*

Diabetes mellitus is the example *par excellence* of this procedure. In it the results of imbalances in the mechanisms are clearly seen, but the total picture is obscured by the inability to trace the forces responsible for the imbalance back to their origin. Insulin therapy has not solved the problem of diabetes; but it has pressed the problem back to the causes of insulin deficiency.

Alimentary glycosuria is not an inevitable result of overindulgence in carbohydrates and its appearance in certain individuals under certain circumstances cannot be explained alone by saying that there is a low carbohydrate (sugar) threshold in the kidney.

One hundred and eighty milligrams per cent of sugar in the blood is no more a fixed point at which sugar must overflow through the kidneys than many other relative standards. Rarely, if ever, can the blood sugar of a normal individual be elevated to this point and

when it is there must be a strong suspicion that some factors other than excessive carbohydrate intake are at work.

On the other hand a spill-over resulting in glycosuria at blood sugar concentration less than 180 mg. is probably abnormal. The situation is only further masked when stress is laid on the conception of a renal threshold for sugar for it still remains unproven that there is such a thing as a true renal threshold.

From these few indications it is evident that the carbohydrates can initiate abnormal processes.

Even before absorption, the carbohydrates in the food can be influenced by other categorical factors with the production of abnormal changes such as excessive fermentation. Such an effect is seen constantly in the fermentative dyspepsias.

After absorption a still larger number of causative factors may become involved because of the many opportunities presented for them to act. Thus hereditary factors may operate in the mechanisms of diabetes; infection can produce changes in tissues where some phases of carbohydrate metabolism are taking place; psychobiologic and bio-social factors can operate through the nervous system and glands of internal secretion to derange balances of glycogenesis and glycogenolysis; certain chemicals and poisons possess the power of influencing carbohydrate usage; traumatism of a demonstrated area of the mid-brain results in hyperglycemia.

The interplay of the primary categorical causes must ultimately explain the entire picture of normal and abnormal carbohydrate metabolism.

The prevention of disease conditions which arise from errors of the carbohydrate supply and its primary utilization should be highly practical. Prevention of more serious derangements of carbohydrate metabolism such as diabetes, can unquestionably be solved when more is known of their natural histories and all the factors involved in their etiology.

CHAPTER IX.

THE NUTRITIVE ELEMENTS IN HEALTH AND DISEASE (CONTINUED).

FATS.

FAT is a compound of carbon, hydrogen and oxygen in which the carbon and hydrogen are not in the proportion to form water, and are in a higher relative proportion to the oxygen than in the carbohydrates. For the latter reason it burns with an energy value over double that of the sugars and starches, each gram yielding 9.3 Calories.

It is presented to the body in animal and vegetable foods and the fats from both classes of food are equally effective sources of energy. The natural foods contain fats largely in the form of neutral fats but also as fatty acids and cholesterol.

The total fat content of some common foods is listed below.[1]

Cereals.	Per cent	*Dairy Products.*	Per cent.
Wheat and barley flour	1 0	Eggs	9 5
Oatmeal	8 0	Milk	3 7
Barley meal	2 2	Butter	85 0
Rice	0 3	Cheese	30 0
		Margarine	83 5

Meat.	Per cent.	*Miscellaneous.*	Per cent
Beef	22 5	Lard	94 0
Veal	6 3	Fresh fruits	0 4
Mutton	24-30	Nuts	22.8
Bacon	60 0	Potatoes	0.1
Ham	31 0	Shelled peas and beans	0 5
Poultry and game	9 5	Dried peas	1 3
Fish (fresh)	1 0	Cocoa	34 0
		Olive oil	100 0

Foods Richest in Cholesterol are:

Egg yolk, brain, fats, cream butter, pork, bacon, liver, kidney.

Digestion of Fats.—The fats, like the proteins and carbohydrates, must first be prepared before they can undergo absorption through the semi-permeable membrane of the intestinal tract.

Most of the fat in the dietary is freely available and the ordinary processes of mastication and gastric activity prepare the bolus of food for immediate action by the intestinal enzymes.

The final forms to which they must be reduced for absorption

[1] Wright, Samson Applied Physiology, Oxford University Press, 1934.

are fatty acids and glycerol. Cooking aids slightly in hydrolysis and a small amount of reduction takes place in the stomach. The active process, however, is limited almost entirely to the mixture of secretory products present in the upper intestinal tract and known as succus entericus. In this flux, the fat is hydrolyzed by the pancreatic enzyme lipase with the aid of the alkaline juices and the presence of bile. In this hydrolysis 1 molecule of neutral fat is reduced to 1 molecule of glycerol and 3 molecules of fatty acid. In the process each fat globule comes in contact with the alkaline bases of the succus entericus and its lipase content. The fatty acids, formed by the action of the lipase are saponified by the alkaline bases and a thin layer of soap is formed thereby on the surface of the globule. Emulsification of the whole fat mass results from the eventual saponification of the individual globules. The bile in the succus entericus brings water into the reaction by its hydrotropic effect and so dissolves the fatty acids and soaps and acts as a diffusing agent. The saponified fatty acids of each globule are now soluble and can penetrate the lining epithelium of the intestine. As the fatty acids are removed from the surface of the globule the lipase can act on their renewed surfaces to form more fatty acids and continue the process. In the absence of pancreatic juice about 50 to 80 per cent of the fat is lost in the feces. When bile also is absent 80 to 90 per cent is lost. Although hydrolysis can take place without the presence of bile, absorption is lowered because of loss of the diffusing power of the bile. Cholesterol may be absorbed directly by entering into solution with the bile salts. The absorbability of fats in general is in proportion to their solubility in bile salt solutions.

Any alterations in the bile content of the small intestine will be seen therefore to exert a strong influence on fat digestion. A compensatory mechanism is present to assure the presence of bile during fat digestion. Either some component of fat acts directly on the sphincter Oddi of the ampulla of the common duct and causes it to relax and allow the flow of bile into the intestine, or the fat meal causes the liberation or formation of some secretory product of the intestinal mucosa which can bring about the same results.

Assimilation of Fats.—Absorption of soluble fatty acids, soaps, cholesterol and glycerol takes place directly through the epithelial cells of the intestinal villi; that is, these products actually enter into the cell bodies. Within the cells the absorbed materials are resynthesized to neutral fats. The exact processes involved between resynthesis and the appearance of fat globules in the lacteals are not known. Present interpretation inclines toward the belief that the fat accumulated in the cells of the villi is discharged into the tissue spaces where the globlets are phagocytized by reticulo-endothelial cells and they are then transported within these cells to the lacteals and are subsequently liberated into the lymph to

form the milky fluid of the lacteals and thoracic duct known as chyle. That synthesis must have occurred is evidenced by the preponderance of neutral fats in the chyle whereas it is known that the fats are not absorbable by the mucous membranes. Cholesterol apparently passes through this cellular activity unchanged.

The chyle of the lacteals is carried forward to the thoracic duct and emptied into the venous circulation by the pumping action of the lacteals, intestinal movements, intra-abdominal pressure changes during respiration, and a negative pressure in the great venous vessels into which the thoracic duct empties.

The fats are absorbed slowly from the intestine as shown by the fact that the lipoid content of the blood does not reach its maximum until six or eight hours after the ingestion of a fatty meal.

The following lipoids are found normally in the blood:

1. Neutral fats (triglycerids) as fatty acid compounds in the plasma and cells.
2. Free cholesterol. Largely absorbed as such from the foods but some resulting from tissue breakdown.
3. Cholesterol esters (cholesterids). Cholesterol combinations with fatty acids.
4. Lecithin (phospholipin). Fatty acid (stearic acid) plus H_2PO_4 and choline (a nitrogenous constituent).

Metabolism of Fats.—The normal blood cholesterol is placed between 140 and 200 mg. per 100 cc. of blood, of which 50 to 75 per cent is in the form of esters. It is probable that cholesterol derived from endogenous sources is a metabolic end-product. Its ultimate fate is unknown and there is no evidence as to how it is eliminated. Even the cholesterol discharged with the bile is largely reabsorbed and reutilized, only a small per cent being lost in the feces as coprosterol.

The postabsorptive blood level of cholesterol is little affected by the amount of fat consumed. What little rise there is seems to be largely accounted for by an increased flow of bile initiated by the fat meal and a consequent reabsorption of more cholesterol. Lecithin restores its normal level eight hours after a heavy fat meal. The actual disappearance of cholesterol and neutral fats from the blood is probably brought about by tissue activity, especially in the liver and the tissue-fat deposits. Cannon believes that it is always by segregation, that is, cellular activity, and never by inundation as is the case with water and sugars. An enzyme has been postulated for this exchange but never demonstrated.

The depot fat of adipose tissue is 90 per cent neutral fat and is obtained from the fat of food and by synthesis from the carbohydrates and the carbohydrate fractions of proteins and fats.

The liver is 3 per cent fat and apparently performs a definite function in fat metabolism. Experimentation indicates that this is of the nature of desaturation. This implies that the fats must be brought

to the liver to be desaturated before they can be utilized for energy. In this connection Bloor[1] believes that lecithin is the form in which fat to be utilized is transported about the body. He points out that lecithin is the only non-toxic compound of the fatty acids which can mix with water.

Why and how fat is released from storage is not known. Kastle and Loevenhart[2] favor the view that it is a mechanical reversible enzyme action in which the enzyme is activated or inactivated by a high or low blood-fat level respectively.

Fat must be burned for the release of its energy. In the section on the processes of carbohydrate metabolism it was indicated that the fats burned only in the presence of an adequate amount of carbohydrate. Because incomplete combustion of fats results in the formation of poisonous ketone bodies (beta-oxybutyric and aceto-acetic acids) and reduction to or below this stage depends on a necessary amount of carbohydrate consumption the ratio between the fats and carbohydrates is referred to as the ketogenic-antiketogenic ratio. Actually it is the total fatty acid-total glucose ratio and is expressed as a fraction of fatty acids over glucose. Ketone bodies accumulate when $\frac{\text{molecules of ``anti-ketogenic'' substances}}{\textit{molecules of ``ketogenic'' substances}}$ equals more than 2.

To make sure that this ratio in the diet is not more than 2, the total fat intake should be less than the sum of twice the carbohydrates plus one-half the proteins ($F = 2C + \frac{P}{2}$). The average fat in the adult diet of 3000 calories is 70 to 100 grams a day.

Effects of Disturbed Fat Metabolism.—The pathologic physiology and pathogenesis of a number of disease conditions reveal disturbances in the storage and use of fat: in atherosclerosis there is an increased amount of fat in the arterial walls without any demonstrable increase in the blood cholesterol level except in the aged; xanthomatosis is generally associated with a hyperlipemia and this in turn is most commonly observed in long-standing cases of obstructive jaundice, nephrosis and diabetes, or it may occur idiopathically; fatty degeneration of almost any tissue shows a "settling out" of fat particles, that is, they become stainable by osmic acid which is not true of the fat content normally found in healthy cells; the blood-cholesterol in nephrosis is not infrequently as high as 500 to 700 mg. per 100 cc. and it has been pointed out that this increase is directly proportional to the increase of serum albumin. The suggestion is made that this may be a response to maintain the osmotic pressure within the blood-vessels. Cholesterol esters are low in many hepatic diseases, supposedly indicating an impaired activity of cholesterol esterase in the liver; gall stones may be composed

[1] Bloor: Physiol. Rev., 2, 106, 1922.
[2] Kastle and Loevenhart: Am. Chem. Jour., 24, 491, 1920.

almost entirely of cholesterol but there is no justification for assuming that they originate from a high blood cholesterol; Schüller-Christian disease shows localized xanthomata and a hypercholesteremia, the causes of which are not known; immunity and susceptibility to infection are allegedly bound up with cholesterol increase or decrease respectively.

It must be admitted that little is known of the rôle of the fat mechanisms in most of those diseases where it seems to be involved. Almost nothing is known of the end of the cycle of fat usage and very little more about the intermediate mechanisms. In none of the diseases mentioned above can satisfactory causal relationship be demonstrated between the findings and the processes of fat metabolism.

The relatively constant lipoid level of the blood, the actively mobile storage depots at various selective points in the body, and the remarkable conservation of bile salts and cholesterol in the biliary cycle, are suggestive that the fat mechanisms are as highly or more highly complicated than those of the carbohydrates. It is certain that the present evidences of deranged mechanisms constitute but a small part of what will ultimately be revealed.

The importance of an adequate amount of fat in the diet may be shown in a summary of its functions:

1. Fats are essential parts of all cells. Although they may be synthesized from carbohydrates this source cannot substitute indefinitely for exogenous fat.

2. Fats are potent sources of energy. Their storage from food fats under normal conditions, and their synthesis when fat is unavailable, indicates that this laying-by is an important mechanism in the body economy. Fats also act as protein sparers with but little loss of energy since their specific dynamic action is only 6 per cent.

3. Fats stimulate bile flow which is important in mechanisms other than their own hydrolysis and absorption.

4. The neutral fats are sources of some of the vitamins.

Categorically, fat defects in the food supply can result in derangement of subsequent fat mechanisms. Fat indigestion is a common occurrence and in most instances must be attributed to abuse of the fats themselves. It results largely from the excessive intake of fats and their influence in delaying the emptying time of the stomach.

Although there is little on which to base the belief that excess of fat may result in metabolic diseases, ignorance of fat metabolism in general forces an open mind on the subject. The sclerotic changes in the vessels of diabetic subjects is alone enough to justify serious consideration of this whole question. It may also be worth while to investigate the rôle of fat derangements in the so-called idiopathic or normal ketonuria of infants.

CHAPTER X.

THE NUTRITIVE ELEMENTS IN HEALTH AND DISEASE (CONTINUED).

INORGANIC SALTS AND MINERALS.

THE mineral constituents of the body are distributed disproportionately among the tissues in response to different tissue needs. It has only been by careful quantitative analysis of the many tissues and organs that an idea has been gained as to the actual amount of each in the entire body.

The stay of a specified amount of a mineral at any one place is probably very temporary because the molecules are constantly being transported, the rapidity with which they are moved depending on the functional state of the process in which they are involved. As with water and other nutritive elements the molecules are eventually caught in some secretory or excretory mechanism and lost to the body. The storage reserves of the mineral elements are quite meager, with the exception of calcium and phosphorus, and their loss must be made up from the outside, that is, through the food supply. For this reason the body is probably always dealing with changing amounts of the minerals and estimates upon them cannot be too rigidly defined.

The total mineral content of the body is estimated at an average of 4.3 to 4.4 per cent by weight. The minerals exist as organic and inorganic salts, acids, bases, free electrolytes, and in complex organic combinations. When they undergo transportation they may be carried in solution or in suspension in fluid media or within migrating cells. Even when they are contained inside of cell membranes they are probably not static but are being moved about in the processes of cell metabolism. Irrespective of where they may be found they are intimately connected with the body fluids, whether circulating, inundating or intracellular.

The metabolism of minerals depends largely on physico-chemical processes. The most prominent of the latter are those which depend on whether the mineral combinations are in the electrolytic or colloidal states. As each mineral element passes through the body it is constantly brought into situations where its use depends upon whether it can pass through a semi-permeable membrane. Upon the permeability of the minerals rest many of the mechanisms of health and disease: it is of the greatest importance in the economy

of the individual cell in relation to its environment; it manifests itself in the disturbed states of tissue and cell readjustments in disease processes that affect the permeability of membranes, the concentration of electrolytes, and the physical state of the colloids. The behavior of the substances on either side of a semi-permeable membrane, by which they bring about molecular balance between them, is represented by Donnan's Law of Equilibrium. (For an excellent elucidation of this law the reader is referred to Trumper and Cantarow's "Biochemistry in Internal Medicine," W. B. Saunders Company, 1932).

Sodium, potassium, calcium and chlorine (as the chlorides) are the elements entering most largely into the osmotic balances and acid-base equilibrium of the body. Sodium is the predominating base in the fluids outside of cells and potassium is predominant within the cells. Chlorine is present as the chloride radicle of both sodium and potassium salts (and in combination with many other ions as organic and inorganic compounds) and therefore participates in many extra and intracellular reactions.

Sodium and Chlorine.—A brief consideration of the combination of sodium and chlorine as sodium chloride will reveal many of the processes dependent upon the supply of these two elements in the tissues and in the food.

The average diet contains an amount of sodium chloride greatly in excess of the body needs. The estimated daily requirement to make up for excretory loss is 1 to 2 grams whereas the average daily consumption is between 8 and 10 grams. Evidently there must be some gross mechanism by which this overabundant supply is cared for because the sodium chloride content of the great fluid matrix, the blood, remains relatively constant at all times. Whole blood has between 450 and 500 mg. of sodium chloride per 100 cc. and this can be little changed by excess or deficiency of salt ($NaCl$) in the diet unless it is continued over a long period of time. This fine adjustment appears to be dependent upon a coarse adjustment outside of the circulating fluids. All of the evidence points toward a storage and excretory balance, the storage taking place largely in the subcutaneous tissue (but also in other tissue-space fluids) and the excretion being cared for in large part by the glomeruli of the kidneys. In both there is an intimate dependence on the water supply and the mechanisms of water and salt equilibrium are looked upon as being similar in many respects.

On the tissue side there is, according to Cannon, a manifestation of his principle of inundation. According to this, the salt is taken out of the circulating fluids and put into the slow moving, almost stagnant tissue fluids in selected areas. The primary factor influencing this exchange is a demand for molecular equilibrium between the two fluids and their crystalloid-colloid contents. This again is

evidence of osmotic balance or Donnan's equilibrium across semipermeable membranes of the tissues involved. Since water is essential for the process and since the water content of plasma and tissue fluids has been shown to be variable, the water and salt exchanges must be interdependent. An excess of water over salt in the tissues will result in the flow of water from the tissues in exchange for salt in the plasma. An excess of salt in the plasma will have the same effect. If for any reason, there is an excess of salt or water brought to those areas in which inundation chiefly occurs there will be an adjustment to correct the imbalance and salt storage or withdrawal will take place to meet the situation. This exchange must go on constantly. Tissue fluids are never entirely stagnant and other processes of cellular metabolism in the inundated tissues are always demanding salt and water. Storage is therefore only a relative conception and it is the *total chloride* content of the body that must be taken into consideration for a proper understanding of the sodium chloride storage mechanism.

At the excretory end of the mechanism the capillary tufts and epithelium of the glomeruli, and the cells of the urinary tubules of the kidney show selectivity for ions of solutes brought to them. For sodium ions, an excess of 0.3 per cent in the solution results in their passage through the excretory apparatus of the kidney and their elimination in the urine. In their passage down the urinary tubules they are reabsorbed by the epithelial lining cells when their concentration in the urine is the same as that in the blood.

This is evidence of conservation of sodium chloride and it probably takes place in health only when conservation is necessary.

Sodium and chloride are also lost to the body through sweat, tears, gastric juice, bile and intestinal mucosa. Except for those situations in which the loss is irrevocable as in tears, sweat and feces, there is evidence of reabsorption. The bile and pancreatic juice together contain as much sodium as the blood plasma and a considerable amount of this is conserved under normal conditions by reabsorption. Gastric juice requires chloride for its manufacture but in this process also some of the chloride is eventually salvaged. In pathologic states large quantities of both sodium and chloride may be lost through rapid elimination by vomiting, purgation and sweating.

Deprivation of salt (NaCl) intake results in lowered salt content of the materials coming from the intestinal lymphatics. This disturbance is carried to the liver and then to the general circulation and is perpetuated as long as the adjustment mechanisms are unable to cope with it. When the deficiency is so great as to be unadjustable within the supply itself the disequilibrium must be cared for by drawing upon the salt storage, and conservation through diminished

elimination. The latter occurs automatically when the plasma content of Na ions falls below 0.3 per cent.

Prolonged deprivation may result in serious consequences because of the withdrawal of NaCl from the tissues (60 to 90 per cent of the tissue loss is from the skin). Diuresis by drugs only adds to the loss and is therefore contraindicated under such conditions.

It is possible to produce excessive salt absorption, especially in children, which results in a condition known as "Salt fever."

The combined regulation of salt and water intake is indicated in some forms of overweight. This has its practical application in weight-reducing diets to be discussed later.

Sodium is present in the body in combination with many ion radicles. As $NaHCO_3$, Na_2HPO_4, NaH_2PO_4, it is concerned in the acid-base regulations in which it keeps up a constant interchange of its acid and alkaline components. The sodium ions are readily interchangeable with many others so that that which was originally absorbed as sodium chloride may soon after absorption become a carbonate or phosphate. This interweaves the two processes of osmotic pressure and acid-base balance so inextricably that they cannot be conceived of *in vivo* as independent mechanisms. Thus the homeostasis of one element in any one of its mechanisms is a function of the homeostasis of the body as a whole. This same principle must apply in the discussion of every other mineral element.

The main source of sodium and chlorine in the diet is in the form of their simplest combination as common salt or sodium chloride (NaCl). The sodium content of the main food sources of this element estimated as parts Na_2O per 1000 parts of the dried substance are:

Beef, 3.0; milk, 1.10; potatoes, 0.3; wheat, barley, rye, 0.1 to 0.4; peas, 0.2; beans, 0.12; apples, 0.1; rice, 0.03.[1]

The chlorine contents are:

Cows' milk, 1.60; white of egg, 1.32; beef, 0.28; potatoes, 0.13. The amounts in other foods are negligible in relation to the bulk in which they are consumed.

Potassium.—Potassium is the element of greatest importance within the cells. It is the only radio-active element of the tissues and this quality may be of extreme importance in certain physiologic and pathologic conditions.

There is apparently no demonstrable storage for potassium other than that represented by its combinations within tissue cells. In order to reach the cells however it must have existed in the circulating fluids and that this is so is shown by its presence in the blood and its active participation there in the acid-base mechanism. But it is only within the cells that it reaches its necessary concentration.

[1] Friedenwald-Ruhräh: Diet in Health and Disease, Philadelphia, W. B. Saunders Company, 1922.

This concentration depends on the passage of electrolytes through cell membranes, retention of colloids (albuminoids of the plasma and intracellular combinations) and other as yet undemonstrated factors which in all likelihood are part of the changing metabolic conditions of the cell protoplasm and its membrane. Intracellular potassium is the main alkaline buffer against acid tendencies produced within the cells by metabolic activity.

Potassium is constantly being lost by its liberation in the breakdown of tissues and its subsequent elimination through the kidneys. Starvation results in a gradual depletion of the protein content of cells and it appears that with this diminishing protein there is a loss of potassium to maintain the balance between them.

Potassium is of special value in the contraction of muscles, and is joined in this function by sodium and calcium. It is also believed to be one of the media through which vagus stimulation affects the contraction of cardiac muscle.

The average intake of potassium in the diet is 2 to 4 grams, obtained largely from the animal and vegetable foods.

Parts of K_2O per 1000 of the dried food substances are: Potatoes, 20 to 28; strawberries, 22; beans, 21; beef, 19; milk, 9 to 17; oats, wheat, barley, rye, 5 to 6; rice, 1.[1]

The exact amount of potassium required per day cannot be given. It is very unlikely that it can be taken in harmful amounts in even the most extreme types of diet.

Excessive intake may temporarily elevate the blood potassium concentration but this is soon reduced to normal (19.5 mg. per 100 cc. serum) by being taken up by the tissues. The physiologic limit of intake has not yet been definitely determined. In health no serious harmful effects have been observed even in daily amounts as high as 50 grains.

The evidence that there is a mutually adjustable ratio between the amounts of sodium, potassium, calcium and magnesium in the total base of the body probably explains in part why wide ranges in the amounts of sodium and potassium consumed do not produce more harmful results.

Calcium.—Calcium is one of the most widely distributed elements in the body and is probably found in every tissue. This is a general indication of diversified function. In the bones, as CaO, it constitutes between 270 to 500 parts per 1000 of the fresh substance; in the muscles, 0.9 to 0.18; nervous tissue, 0.03; liver, 0.36 to 0.03; blood plasma, 0.06 to 0.08. In the normal blood it averages 10 mg. per 100 cc.

Knowledge of calcium metabolism is limited to a few estimations

[1] Friedenwald-Ruhräh: Diet in Health and Disease, Philadelphia, W. B. Saunders Company, 1922.

in certain tissues under experimental and disease conditions. From these a few important inferences have been made.

It has been mentioned previously that calcium is stored temporarily in the bones. This is accomplished by the process of segregation in which certain wandering cells in the trabeculæ have the power of taking up calcium from the fluid media surrounding them and holding it in the bone tissues.

Where it was formerly thought that the calcium was laid down in osseous tissue once and for all it is now known that this deposit is only relatively stationary. The specialized cells which hold the calcium and build up the bony skeleton are called osteoblasts. Other cells, the osteoclasts, act as phagocytes and remove the calcium from storage. It is believed that by these two processes the deposits in one portion of a bone are being constantly shifted about in their immediate neighborhood and even to more distant parts of the same bone. The cause of this continued disturbance has not been demonstrated.

This shifting storage of calcium is in response to bone and other metabolic needs. From a study of these needs it is found that the calcium stored in bone has an antecedent history in which the calcium in transportation partakes in other functions before it becomes segregated, and also that after segregation it is again transported to satisfy further needs.

Following absorption from the intestine in the form of the soluble sulphate and carbonate these calcium compounds participate in the acid-base equilibrium and the degree to which they do so is in proportion to the amount of calcium in the ionized form. The latter in turn is dependent on the ratio of the two physiologic states in which calcium exists in the serum, that is as diffusible or non-diffusible calcium. It is believed that the latter is non-diffusible because of its combination with serum protein.

Calcium which is carried to the muscle and nerve tissues is physiologically active in the phenomenon of irritability in these structures. It is also concerned with the permeability of capillaries, and enters into the mechanism of blood coagulation by speeding up the action of thrombokinase on prothrombin. Calcium is an important element in the formation of milk.

Calcium excretion is by way of the urine and feces, 10 to 15 per cent being lost by the former and 85 to 90 per cent by the latter. The thyroid gland is believed to participate in some manner in calcium excretion.

A few of the factors which influence the utilization of calcium must be reviewed in order to indicate the part which they play in normal and abnormal metabolism.

The absorbability of ingested calcium depends on three factors: the degree of acidity of the upper intestinal tract; the presence of

vitamin D.; the calcium-phosphorus ratio. More soluble salts of calcium are formed in an acid medium. When the acidity is low or the reaction is alkaline in the upper intestine more insoluble calcium salts are used in the formation of soaps and this calcium is lost through the feces. Vitamin D aids absorption in some still unknown manner. Calcium phosphate is more readily absorbed than the carbonate. Moreover much of the physiologic effect of calcium is dependent on the amount of phosphate in the serum.

In health the serum-calcium remains at a fairly constant level of approximately 10 mg. per 100 cc. This is maintained by a balance between absorption, storage, liberation, and excretion. The two most active factors known to be concerned in maintaining this level are the secretion of the parathyroid glands (parathormone) and vitamin D (or ultra-violet irradiation). The former when overacting raises the blood calcium level, due, at least in part, to its stimulating effect on osteoclast formation which in turn, increases the liberation of stored calcium. Vitamin D may act in a similar direct manner or by stimulating the parathyroids; or it may raise blood calcium by increasing absorption. Which of these is the correct explanation must await further investigation. Some believe that vitamin D (or ultra-violet irradiation) is essential for parathormone efficiency.

A low serum-calcium is brought about by parathormone or vitamin D deficiency.

On the basis of these facts, rests the probable explanation of a number of disease phenomena.

Osteitis fibrosa cystica (von Recklinghausen's disease) is associated with a high serum-calcium and adenoma of the parathyroid gland. If this latter means overactivity it is reasonable that there is increased osteoclast activity, liberation of stored calcium, and elevation of serum-calcium.

A high calcium level may result from hypervitaminosis-D and this interesting clinical observation is under investigation.

Rickets is the outstanding condition representing defective calcium metabolism. The absence of vitamin D or ultra-violet radiation interferes with calcium absorption and bone formation. This results in the characteristic clinical findings which need not be reviewed here.

Osteomalacia is another disease which shows loss of bone-calcium deposit and may or may not show lowering of blood calcium. It is seen in women after repeated pregnancies and in conditions favoring poor nutrition. There is strong indication that it is due to deficiency in vitamin D in some cases, and probably the parathyroid secretion is involved directly or indirectly.

Many other conditions could be cited in which calcium metabolism is involved. For them it may be said in general that the de-

rangement is not of the primary utilization type but of the nature of changes in the distribution of calcium in the body, alterations in the proportion of diffusable and non-diffusable calcium in the blood, chemical and physical states which interfere with calcium absorption or excretion, and shifting of the calcium-phosphorus ratio in the serum.

To maintain calcium balance the average daily requirement is 0.9 to 1 gram. The mechanisms of calcium utilization prior to absorption in the upper intestinal tract result in a heavy loss of the total amount ingested. This has been estimated to be around 75 per cent of the intake and is eliminated in the feces. As a result the average diet should contain an original high calcium content. Sherman's investigations on American diets found that 15 per cent of them were below calcium requirement. Milk with a calcium content of 1.4 gram per liter is the best single source for this element. The milk products, cheese (5 to 10 grams per liter) and butter, are the next in order of importance.

PERCENTAGE OF CALCIUM IN THE TOTAL ASH OF COMMON FOODS[1]

Fruits	30–7	Vegetables	27–5
Berries	14–8	Milk, egg, cheese	35–8
Nuts	9–8	Meat and fish	18–7
Cereals	8–7		

[1] Friedenwald-Ruhräh: Diet in Health and Disease, Philadelphia, W B Saunders Company, 1922.

Since calcium absorption is favored by an optimum amount of vitamin D, an efficient fat mechanism in the intestine, and an acid medium, these factors must always be taken into account when attempting to regulate its intake. There is some evidence that the average requirement of calcium is not necessarily the optimum for the organism. That is, if the calcium-phosphorus ratio of the blood serum is kept normal (ratio index 50 to 60) the calcium may be used in excess of average requirements with additional advantage to the organism as a whole. In health it is probably impossible to create any strains on calcium metabolism which would be harmful. No practical dietaries can therefore be said to possess calcium in excess of the body's regulatory mechanisms.

A deficiency of calcium in the diet may bring about depletion of the stored calcium in the body. In the mechanisms reviewed above it was seen that when the intake of calcium was lowered the serum-calcium level was not changed because the stored calcium was mobilized and brought into the blood stream. This "transported" calcium undergoes quantitative reduction by its loss through the kidneys and intestines. To make up for this loss more calcium is withdrawn from the tissues and the negative calcium balance becomes more and more accentuated.

This understanding reveals the need for keeping up a sufficient

calcium supply in the diet of growing children and pregnant and lactating women, in all of whom the daily demand is high.

Phosphorus.—In the average individual of 140 pounds (70 kg.) there are about 1400 grams of phosphorus stored in the bones, 130 grams in muscle and 12 grams in brain and nerve tissues. Expressed as PO_4 the blood plasma contains 3 to 5 mg. per 100 cc. It is heavily concentrated in the red cells which contain 85 mg. per cent.

With the exception of its participation in the formation of nucleoproteins, phosphate esters, lecithin and phospholipins of cells, the metabolism of phosphorus closely parallels that of calcium. Thus, its absorption from the intestine depends upon the influence of vitamin D, the acidity of the intestinal contents, the amount and utilization of fats, and the calcium-phosphorus ratio. When absorbed it constitutes one of the buffers in the mechanisms of acid-base balance. It probably is the chief buffer in combating acid tendencies within the cells.

The kidneys convert the free-circulating basic phosphate to the acid form which is eliminated in the urine. In this mechanism the base radicle is reabsorbed by the kidney tubules and restored to the blood serum. This is one of the important processes in maintaining acid-base equilibrium in acidosis.

Before the absorbed phosphorus becomes segregated in tissue cells, or after it has been liberated from storage, it is believed to play some part in the intermediate metabolism of the carbohydrates. This is evidenced by its presence as hexosephosphates in serum and tissues, and by the reduction of serum phosphorus in diabetes under insulin therapy.

The storage of phosphorus by segregation takes place largely in the bones but it is also found in considerable amounts in the muscles, brain and nerves as shown by the analysis at the beginning of this section.

In the bones it is in the form of calcium phosphate. Little is known as to how phosphorus becomes stored other than through the indirect evidence brought out in the study of calcium metabolism. That the concentrations of calcium and phosphorus are mutually dependent upon each other has been adequately demonstrated and it is believed that anything which augments the concentration of one forces out the ions of the other and permits the former to be stored in the bone. Such belief is enhanced by the fact that the serum in respect to both these elements is supersaturated at the centers of calcification, probably the result of accumulation of an enzyme (phosphatase) at these points.

Phosphorus is eliminated in greater part ($\frac{2}{3}$) through the kidneys. The remainder is lost in the feces.

The amount of phosphorus in the body is dependent largely on the degree to which the intake in food is absorbed. On this principle

it is now generally assumed that those conditions which favor its absorption will increase its concentration, and then its utilization, provided the calcium is not simultaneously increased. In this way vitamin D, irradiation and acid conditions in the intestine will aid absorption, but if the calcium of the diet is also high, it is absorbed better for the same reasons and the phosphorus is largely eliminated in the urine. This mutual exclusiveness is behind the statement that the calcium-phosphorus ratio is of more importance than the actual amount of phosphorus supplied.

On the basis of these mechanisms a hyperphosphatemia may result from; (1) excessive vitamin D or ultra-violet radiation; (2) hypoparathyroidism in which the fall in serum-calcium is accompanied by a rise in serum-phosphate; (3) retention in nephritis; (4) healing fractures with increased storage of calcium in the repair process. Conversely, hypophosphatemia will be found in; (1) diminished absorption from lack of vitamin D or ultra-violet radiation; (2) rickets with a calcium-phosphorus ratio of less than 30; (3) osteomalacia, probably also due to vitamin D deficiency; (4) hyperparathyroidism, by increased elimination in the urine.

The highest phosphate-bearing food is yolk of egg. It is found as inorganic phosphate in milk and animal cells and in organic combination as nucleo-protein, phospho-proteins, and phospho-lipins of nerve tissue, liver and pancreas.

Sherman estimates that an intake of 0.9 gram per day will maintain phosphorus equilibrium. In order to allow for loss by failure of absorption the optimum daily supply should be nearer 1.5 grams.

An average balanced diet which fulfils the requirements in other respects can hardly result in phosphorus deficiency. It is of more importance therefore to consider the other elements of nutrition for in doing so the phosphorus will take care of itself.

Iron.—The iron circuit in the body is poorly understood other than through inferences made from its presence in certain tissues and its action in some of the part-mechanisms in which it is concerned. It is the connecting links between these isolated phenomena that are not yet known.

The total amount of iron in the average adult body is estimated at 3 to 4 grams. Although the tissues of the new-born infant contain iron obtained from the mother this supply becomes exhausted through the natural destruction of red cells and by elimination. It is essential that this loss be made up through the diet which is the only possible source from which it can be obtained.

Iron is presented to the body as organic and inorganic compounds of animal foods and in vegetables and fruits. Most of it is in the form of complex organic combinations but the simpler ferric and ferrous salts are also available. Present evidence indicates that only non-hematin iron can be used in the formation of hemoglobin.

Absorption of iron takes place in the acid medium of the duodenum and in the upper part of the small intestine. This apparently is accomplished by the vital activity of the lining cells of the intestine, or by leukocytes.

After absorption iron is next seen in the liver where under normal conditions it is stored by segregation in the reticulo-endothelial elements. In conditions of excess the iron can also be found in the parenchyma and Kupffer cells of this organ.

At some time in its metabolism the iron is taken into the cell body of the erythrocytes and probably also of all tissue cells. Although iron appears to be an essential ingredient of the cytochrome of all cells that use oxygen, the total amount in the tissues of the body must be slight in comparison to that in the red cells which are estimated to hold 90 per cent or more of it (3 grams or less). Starling[1] describes the function of the iron-containing cytochrome as that of "the middle man, conveying oxygen from the air to take up the hydrogen set free by the action of dehydrases of the tissues."

Within the red cells, iron is mostly in the organic combination known as hemoglobin, a protein compound. It is in this form and position that iron seems of greatest use to the body for hemoglobin possesses the property of reversible oxidation and reduction. On this property depends its function in the exchange of oxygen and carbon dioxide in the lungs and tissues. The iron component appears to be essential in this process.

Hemoglobin, and therefore iron, plays an important part as a "buffer" in the acid-base regulatory mechanisms.

It is known that erythrocytes are constantly being formed and destroyed and it is undoubted that iron is involved at both extremes of red cell life. Although it has not been definitely proven it is widely believed that iron acts as a stimulus to the blood-forming organs to produce those cells in which it will ultimately be used. Destruction of erythrocytes liberates simple organic iron. The appearance of large quantities of iron in the spleen, the "graveyard of the red cells," is generally taken as indicating that this is iron which has been stored following its liberation by red cells. The relationship between the stored iron in the liver and that in the spleen and bone-marrow has not been ascertained. It is not known which comes first, but it seems that each is available for reutilization. It is possible that some obscure phenomena of blood deficiencies may be found to depend on qualitative deficiencies between these stored funds of iron.

Iron is eventually excreted at some point in its circuitous history, mostly by the large intestine and feces but also in minute traces in the urine. If iron is supplied in great excess in the diet or as medi-

[1] Starling, E. H.: Human Physiology, Philadelphia, Lea & Febiger, 1936

cine the body appears to absorb only as much as is needed and to pass the rest by way of the feces.

If the spleen is removed, storage of iron seems to be interfered with and it is eliminated in increased amounts in the urine. It is not understood why, in this instance, the kidneys take up the greater part of a function ordinarily performed by the large intestine.

In hemochromatosis some disturbance of iron mechanism results in the storage of excessive amounts as hemosiderin in the reticulo-endothelial and parenchymal cells of the liver, pancreas and other tissues.

A deficiency of iron in the diet results not only in a gradual depletion of iron in the body but also a loss of some hematopoietic stimulus. This is observed so constantly in the microcytic anemias of infancy, and in association with achlorhydria in adults that the stimulation of blood formation by iron is almost taken for granted. (Copper may be necessary in this same process.) Discussion of the possible influence of iron in combination with vitamin E on fertility will be found in the section on vitamins.

Even such fragmentary information on the utilization of iron reveals its absolute need for tissue oxidation, the formation of hemoglobin, respiratory exchange, and its probable need for proper erythrocytogenesis. It also shows that a deficient iron supply cannot be tolerated indefinitely and that iron excess is ordinarily automatically discharged.

To make up for iron loss it is essential that the average daily intake for adults should be from 5 to 12 mg. Unfortunately, milk, the most common food for those who need iron most, is inadequate in regard to this element.

THE IRON CONTENT OF SOME COMMON FOOD SUBSTANCES (BUNGE) [1]
(Milligrams per 100 gm. of food)

Rice	1 2	Almonds	9.5
Wheat flour	1 6	Red cherries (without stones)	10.0
Cow's milk	2 3	Apples	13 0
Human milk	2 3–3 1	Cabbage (outside leaves)	17 0
Cabbage (inside leaves)	4 5	Beef	17 0
White beans	8 3	Asparagus	20 0
Carrots	8 6	Yolk of egg	10–24
Strawberries	9 6–9 3		

[1] Friedenwald and Ruhräh: Diet in Health and Disease, Philadelphia, W. B Saunders Company, 1920, p. 162.

In a balanced diet in which the protein intake is sufficient for individual requirements, the iron supply should also be adequate because of the close parallelism between protein intake in grams and iron in milligrams in the protein.

Iron is frequently supplied in medicinal form as a supplement to the diet. Almost every conceivable form of iron has been utilized

including hemoglobin itself and even whole blood. Much has been written about the ability of the body to utilize iron in the different forms in which it has been presented and the matter is still one of controversy. *It is firmly maintained by some, that provided the iron given is in an absorbable state, an excess over requirement will result in increased usage with added benefit to the organism.* There is not sufficient evidence to support this belief.

In regard to the requirement that the iron be absorbable there is accumulating data that may permit the iron salts and compounds to be graded on this basis. Mitchell and Schmidt,[1] and Mitchell and Vaughn[2] classify them in three groups according to their solubility and absorbability:

Especially good.	Fairly good	Poor.
Ferric acetate	*Peptonized ferric oxide*	*Ferric oxide*
Ferric albuminate	Saccharated ferric oxide	Ferrous carbonate
Ferric chloride	Saccharated ferrous carbonate	Ferric potassium tartrate
Ferric citrate	Ferrous iodide	Ferrous lactate
		Ferrum ruductum
		Ferrous sulphate

It is believed that irrespective of the form in which iron is administered in food or medicine it is changed by the stomach secretions into the ferrous and ferric salts.

After absorption these two salts appear to be reversible.

Copper.—The amount of copper in the body is so small and unevenly distributed that no practical purpose could be served by its determination. It is obtained from the copper salts taken from the soil by vegetables and probably exists in traces in animal livers.

Nothing certain is known about its absorption or intermediate metabolism.

So far as its usefulness is known it is apparently limited to participation in the processes of hematopoiesis, hemoglobin formation, and possibly oxidation within the red cells. In the first it seems to act along with iron in the stimulation of endothelial elements of the capillaries of the bone-marrow to progress through the stages of erythrocyte formation. Its point of action is believed to be at the developmental level of erythroblast-normoblast conversion. In the absence of copper this last change from normoblast-erythroblast to erythrocyte is interfered with and the bone-marrow and circulating blood show these low-level red blood cells. This failure results in the presence of large numbers of microcytes and the condition is called microcytic anemia. The actual part played by copper is not known. *Hart, Steenbock, Waddell and Elvejem*[3] *found that copper* in addition to iron was necessary for the cure of microcytic (nutri-

[1] Mitchell, H. S., and Schmidt, L.: J. Biol Chem., 70, 471, 1926.
[2] Mitchell, H. S., and Vaughn, M.. Ibid., 75, 123, 1927.
[3] Hart *et al.*: J. Biol. Chem., *77, 797, 1928; Ibid., 84, 115, 1929.*

tional) anemia. They claim that reported successes by the use of iron alone are due to the fact that the iron preparation used contained other metals as impurities.

Copper also seems to be of use in the formation of hemoglobin. Nothing more is known than the empiric observation that it appears to assist in the conversion of absorbed iron to hemoglobin.

An indication of the minute traces in which copper may be effective is shown by the conclusions of Chou and Adolph[1] that the daily adult requirement is about 2 mg.

Copper absorbed in excess is apparently retained in large part in the liver as evidenced by Mallory's pathologic studies on that organ in various forms of cirrhosis.

It is probable that any diet containing sufficient iron will also contain the necessary amount of copper.

Sturgis believes that copper need not be given therapeutically because all pharmaceutical preparations of iron are grossly contaminated with this element.

Manganese.—Manganese, in the opinion of McCarrison,[2] is concerned in some way with growth. He found that optimal growth took place on a daily intake of 0.0327 mg.

This mineral is believed to be operative in hematopoiesis in the same manner as copper and that it may be an alternative to copper or some other element. Its deficiency may play a part in microcytic anemia.

In the diet manganese is especially abundant in the outer layers of wheat and is found in cabbage, fruits, legumes, cauliflower, lettuce and grapes.

Magnesium.—Magnesium (as MgO) is found in the following amounts in the body per 1000 parts of the fresh organs listed:

	Grams.
Muscles	0 40
Bone	4 to 6
Liver	0 02–0 007
Blood plasma	0 02 to 0 05
Blood corpuscles	0 07

The normal blood serum level is 1.3 mg. per 100 cc.

Although it is present in greatest amount in the bone it is probable that it is there in storage. The factors influencing its deposition in bone as solid magnesium phosphate and carbonate are believed to be the same as those responsible for the storage of calcium and phosphorus.

Magnesium in transportation in the blood remains at a constant level and no known clinical conditions or extraneous factors seem to influence it. The cause of this remarkable stability in spite of the

[1] Chou, T. P., and Adolph, W. H · Biochem. J., 29, 476, 1935
[2] McCarrison, R., Ind J. Med Res., 14, 631, 1926

several factors mentioned below which will effect its elimination is not known.

An important function ascribed to magnesium by Lehmann[1] is its participation in the transformation of glycogen to lactic acid during muscle activity. He states that it is essential to this process along with an enzyme, a phosphate, and adenyl-pyrophosphate.

Absorption of magnesium takes place in the upper intestinal tract under the same conditions which favor calcium absorption. This Peters and Van Slyke[2] suspect, is due to a similar solubility of magnesium and calcium.

Magnesium is excreted in the urine in the amounts of 0.3 to 0.5 grams daily. The administration of magnesium and acidifying measures increases the elimination in the urine. Holt states that in infants 56 per cent of ingested magnesium is eliminated in the feces.

A further similarity between calcium and magnesium metabolism is evidenced by the response to parathormone and parathyroidectomy. According to Greenwald and Gross[3] the former increases its elimination and the latter causes its retention.

Nothing can be stated about the effect of a deficiency of magnesium in the diet. It can probably be substituted for by other elements so far as the bones are concerned and it is likely that a defective supply may only have some influence on the neuro-muscular mechanism.

Since the daily requirement of this element is not known it will only be practical to name the foods in which it is prevalent with a rough indication of its percentages:[4]

Fruits	8 to 5 per cent (Apples, pineapples, oranges, cherries, pears, figs)
Nuts	18 to 6 per cent (Almonds, walnuts, cocoanuts.)
Vegetables	9 to 5 per cent (Tomatoes, sugar beets, pears, cauliflower, lettuce, spinach, celery, carrots, onions.)
Cereals	16 to 5 per cent (Corn, wheat, barley, rye, oats, rice.)
Meats and fish	9 to 5 per cent (Salmon and pork)

Iodine.—Practically all of the iodine in the human body is found *in and utilized by the thyroid gland. Since it forms an integral* part of thyroxin, the internal secretion of the thyroid, it must be found along with the distribution of thyroxin in the tissues. The total amount in the body is between 10 and 20 mg.; the blood iodine level is 0.011 mg per 100 cc. of blood.

[1] Lehmann: Nature, 19, 180, 1931

[2] Peters, J P, and Van Slyke, D D Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1931.

[3] Greenwald, I., and Gross, J: Jour Biol Chem., 66, 185, 1925, Ibid., 66, 201, 1925.

[4] Friedenwald and Rubräh. Diet in Health and Disease, Philadelphia, W. B. Saunders Company, 1920.

Iodine is absorbed from the small intestine, carried by the blood to the thyroid gland, combined there with amino-acids to form thyroxin, and in this or some closely related form returned to the circulation and carried to the tissues. On the breakdown of thyroxin the iodine fraction is again liberated and returned to the thyroid gland for resynthesis into thyroxin. The body conserves iodine with the greatest economy probably storing it in combination in the colloid material of the thyroid.

The necessary intake of iodine per year to make up for its gradual loss is estimated to be roughly equal to the amount in the body at any one time, *i. e.*, 10 to 20 mg. This makes an average daily requirement of 0.03 to 0.05 mg.

The function of iodine is limited to its presence in thyroxin and the function of this in turn, is calorigenesis. Plummer looks upon it as a catalyzing agent which accelerates metabolism in all cells of the body.

A thorough discussion of the function of iodine is beyond the scope of this work for it would involve a review of all of the functional derangements of the thyroid gland.

The beginnings of some of these deranged functions are due however to defects in the original supply of iodine in the food. An actual quantitative deficiency in the food and water results in the formation of an inadequate amount of thyroxin. This is the basis for the development of endemic cretinism and endemic goiter. The deficiency of iodine in the food can be traced back through the vegetables to the soil of goitrous regions from which a large part of the iodine has been removed by geologic and meteorologic influences. The heaviest endemic areas are Switzerland and the Great Lakes basin in the United States. The water supply of these regions is low in soluble iodides. Sporadic goiter and cretinism in non-goitrous regions is due not alone to a lack of iodine in food but some alteration of iodine usage caused by as yet undertermined factors.

The iodine deficit can be made up by addition of this element to the food either by the consumption of larger amounts of iodine-rich articles of diet or the use of a salt of iodine (generally sodium iodide) as a condiment. It is obvious that the added iodine need be very small in amount from the observation that only 10 to 20 mg. are required in a year. For this reason the deficit is generally made up by giving iodine-containing food the year round or iodine preparations at intervals. In goitrous regions the iodized table salt method is more commonly used or the water supply of the district is iodized.

Iodine in excess may stimulate an already overfunctioning thyroid to still greater activity and produce thyrotoxicosis.

When given to patients with exophthalmic goiter Means believes that iodine simply dilutes the thyrotoxicosis by time, that is, it

alleviates the condition at any one time but does not alter the duration of the disease.

In animal foods iodine is found in greatest amounts in the nucleoproteins. The amount in grams in a kilogram of the raw foods is given in the following table:[1]

Shrimp	5 9	Oysters	1 32
Crabs	1.8	Cod	1.32
Lobster	1.78	Anchovies	0 95
Herring	1.57	Whiting	0.31
Fresh salmon	1.4	Trout	0.08

Grams per Kilogram of Fresh Vegetables.

Green beans	0 32	Rice	0 17
Bananas	0 31	Carrots	0 134
Asparagus	0 24	Leeks	0 12
Garlic	0 21	Green peas	0 80
White cabbage	0 21	Tomatoes	0 23
Mushrooms	0 17	Grapes	0 02
Strawberries	0 17		

In general, it is the sea foods and starchy vegetables which furnish most of the iodine. Because of the presence of relatively large amounts of this element in certain seaweeds this material is quite generally used as a supplemental food.

Those vegetables that show the higher proportions of iodine in the above list may have very much less or none in goitrous areas where the iodine is practically absent in the soil. Under such circumstances the diet alone cannot be adequate and iodine must be supplied by other means.

An excess of iodine obtained from food alone is scarcely conceivable.

[1] Friedenwald and Ruhräh (in part) Diet in Health and Disease, W. B. Saunders Company, Philadelphia, 1920.

CHAPTER XI.

THE NUTRITIVE ELEMENTS IN HEALTH AND DISEASE (CONCLUDED).

VITAMINS.

HISTORICALLY, the term vitamin was applied to designate a class of unidentified nutritive principles, the activities of which could not be included in the known processes by which fats, proteins, carbohydrates and minerals carry out their functions. Although something of their nature had been suspected for several years, it was not until Eijchman, and later Funk showed that one (vitamin B) was a distinct entity, that anyone had an idea as to what they were. The one outstanding point about them which was eventually revealed and for which they were given their name, was that they were indispensable food principles necessary for full vital activity, growth and development of at least the higher forms of life.

When knowledge of the vitamins had advanced to the point of recognizing that there were four of them it was found that a primary classification was possible on the basis of their solubility. Designating them alphabetically vitamins A, B, C, and D, this earliest classification placed vitamins A and D in a fat-soluble group *and vitamins B and C as water-soluble. This distinction is still* retained because of its convenience in laboratory determinations where solubility is a prime consideration and in practical dietetics because fat-soluble vitamins are present only in fat containing foods and the water-soluble group is found in foods with or without fats.

Present information shows that the vitamins are a heterogeneous group of chemical substances that are categorically distinguished by their different functions. Their solubility cannot constitute a permanently satisfactory classification; function, so far, is the only criterion for classification and their chemical composition to date serves only to differentiate them. Evidence has accumulated to show that the number of original vitamins can be extended and that one vitamin may have two or more factors. Opinions differ as to whether the split fractions are to be continued as refinements of the vitamins or are to be designated as new vitamins. The nomenclature now in use reflects both of these ideas. Thus vitamin B is now vitamin B complex. To some this is thought to be made up of vitamins B_1, B_2, B_3, B_4, and B_6. The separatists

call B_2, vitamin G, or P-P, or F. Sherman[1] refuses to define vitamins on the basis that not enough is known about them to permit a definition which will outlast accumulating knowledge.

Experimentation has shown that vitamins are so minute, in the amounts required to produce their effect, that there can be no question of their contributing anything to the body in the way of energy contained within themselves. This neither precludes nor affirms catalytic activity. It is questionable whether vitamins can be synthesized by the animal body. As far as is known, man obtains his vitamins either directly or indirectly from vegetables. Certain indications that some bacteria can synthesize vitamins is taken to indicate that bacteria are probably vegetable. (These borderline states show how precarious hard-and-fast dividing lines may be.)

Precursors of a few of the active forms of the vitamins have been found, some within the body of man and animals and some in vegetables. The activators of these provitamins appear to be as diverse as the chemical nature of the vitamins themselves and range from enzyme activity to the radiant energy of sunlight.

There is enough similarity between the functional aspects of the vitamins and hormones to suggest more than a close parallelism between them. This is based on the evidence that the substances in each of these groups represent a complex molecular integration with living material and that their activities are more than those of catalytic agents.

Sufficient is known about the vitamins to justify their inclusion in a basic category. Because they or their precursors are obtained with the food supply, and their quality and quantity are variable with the availability, preparation and use of foods they have been retained in the category of nutritive elements. It may be possible that further knowledge will eventually place them elsewhere.

The source, special characteristics and functions of the vitamins will be given more specifically in the consideration of the individual vitamins outlined below.

Vitamin A.—The precursor of vitamin A is carotene, one of the plant pigments familiar in one form as the yellow coloring matter of corn, carrots and butter. It may be masked by other pigments and therefore the older belief that the more intensively yellow products are the more potent sources of vitamin A can no longer be held. Refined analysis of carotene by Kamer, Walker, Schopp, and Marf, indicate that there are isomers of this pigment, one of which B—carotene appears to be chemically equivalent to vitamin A ($C_{20}H_{30}O$) and similar to it in action.

Other isomers of carotene and certain carotinoid pigments are

[1] Sherman, H. C. General Review of Our Present Knowledge of the Vitamins, Bull. New York Acad. Med., 10, 457, 1934.

under investigation as to their relation to vitamin A. It is now believed that vitamin A does not occur in plants and that carotene is not found in animals. In the preceding general discussion of vitamins reference was made to the ability of certain bacteria to synthesize vitamins. More specifically, carotene has been demonstrated in bacteria in the intestinal tract of experimental animals but it has not been shown that the bacteria can produce vitamin A from this pigment. It may be found that this carotene can be used by the animal harboring the bacteria when the latter die and break up.

Vitamin A is fat-soluble and is taken into the body in solution in the organic fats. Its presence in animal fats and milk is accounted for by the vegetable diet of herbivores and the small plankton food of fish. These animals convert carotene to vitamin A and store the latter in various tissues, especially the liver. The human is probably able to convert some carotene to vitamin A and this with the preformed vitamin A from animal fats is stored largely in the liver. This store is available during lowered vitamin A intake, but its amount is apparently sufficient for only a matter of a few weeks.

The exact nature of the mechanisms by which carotene is converted into vitamin A is still largely a matter of speculation. Alcott and McCann claim to have brought about the change *in vitro* by treating carotene with preparations of liver. They explain their results on the probability that the liver material contained an enzyme specific for the reaction. This hypothetical enzyme, or enzyme system, has been named carotenase.

The main food sources of vitamin A are shown in the following table: (one, two or three asterisks indicate relative richness in vitamin A content).

Animal Sources.

***Butter	**Beef liver
***Cod-liver oil	**Human milk
***Cream	**Oysters
***Eggs	*Fish
***Cow's milk	*Egg-white
**Cheese	

Vegetable Sources.

****Apricot	**Peas
***Carrots (raw)	**Sweet potatoes
***Spinach	**Pumpkin
***Watercress	**Tomato
**Green beans	**Asparagus
**Breads	*Navy beans
**Cabbage	*Cauliflower
**Carrots (cooked)	*Oatmeal
**Corn	*Parsnips
**Dandelion greens	*White potato
**Lettuce	*Rye
**Orange-juice	*Wheat
**Peaches	

Other vegetable and animal products not listed have insignificant amounts. Little can be said regarding the absorption of vitamin A or carotene from the intestinal tract other than that its passage through the intestinal walls is in conjunction with the fatty acids. Certain oils in which vitamin A may be dissolved form more potently active combinations than others, and natural oil sources of vitamin A are better than refined preparations of the vitamin in oil. This latter observation may be explained by the presence of still unknown active principles in the natural oils.

Vitamin A as found in the natural oils of food is heat stable within the ranges of temperature encountered in the ordinary processes of cooking, canning and preserving. It is also quite resistant to oxidation. In its extracted forms and as concentrates it is believed to be more readily damaged by heat and oxidation.

The daily requirements of vitamin A for man have not been determined. Quantitative assays of cod-liver oil and artificial concentrates of carotene are made by observing the gain in weight of rats on standard vitamin A defective diet in a given period of time. Sherman's unit of vitamin A is that amount which when fed daily to a standard test animal, prepared as described (standard daily weight of rat, etc.), will suffice to support an average gain in body weight of 3 grams per week during the test period of four to eight weeks. An international vitamin A unit has been propósed which is to be equivalent to 0.001 mg. of pure carotene.

In the rat 0.003 mg. has been found sufficient to prevent avitaminosis A. What this may be when translated into human requirements is not known.

Although many inferences have been made as to the rôle of vitamin A in the human organism practically nothing is known of the mechanisms involved. Most that can be known must be obtained by observations on the effect of its deficiency or excess in the diet under clinical or controlled experimental conditions.

From continued observations of this nature the activity of vitamin A has been found to be far more versatile than that originally ascribed to it as the "growth and anti-xerophthalmic" factor. More recently it has been described as being mostly concerned in the maintenance of "health and vigor," but this too is little more than saying that it is indispensable to the maintenance of health. Vitamin A has also been called the "anti-infective agent." All of these designations must be accepted with the reservation that they are tentative, unproven, working terms and that they are probably both true and false, the former because vitamin A does play some part in the functions described, the latter because they impute whole functions to vitamin A in which it is only partly involved. These are all end-results of its action and as such serve only to point to the need of a clearer understanding of the mechanisms involved.

They indicate also how complicated the processes must be for any single agent to institute reactions which can reach such generalized proportions. It is not clear as yet that these results may not mean more than the operation of vitamin A alone but that they may be brought about by the interaction or combined action of this factor with other vitamins and effective agents.

Vitamin A deficiency in young experimental animals leads to lessened growth. It is on the basis of this observation that the designation "growth factor" is applied. Mendel[1] points out that this is not a specific reaction to a deficiency of vitamin A because in young animals a deficiency of almost any of the indispensable nutritive elements leads to arrested growth. That vitamin A can do so is not denied, but this does not make the result specific or unique.

There is increasing belief that the "health and vigor" factors, the "anti-xerophthalmic" effect and the presumed rôle of "anti-infective agent" may all be explained by the influence of vitamin A in maintaining the mucous membranes in a normal condition. This is deduced from the evidence that a deficiency of vitamin A leads to keratinization of mucous membranes. This in turn results in a defective "first line of defense" against invading microörganisms, causes alterations in the physiologic mechanisms of the membranes involved (such as the lachrymal apparatus and respiratory system), and interferes with other processes dependent on the integrity of these structures. Thus ulceration of the cornea may be brought about with secondary infection of the accessory structures of the eye as well as of the eye itself, or the change in the sinus and bronchial membranes may enhance the ability of microörganisms to invade these tissues and set up disease. There is no definite indication that vitamin A has any direct effect on the immunizing powers of the body. The anti-infective effect of this vitamin is looked upon therefore as indirect and probably only reveals itself when its lack in the diet has approached a minimum which is reached only under exceptionally impoverished dietary states.

There is, apparently, a correlation between the amount of vitamin A in the diet and tissues and the ability of the retinal rods to regenerate visual purple. Failure of visual purple results in night blindness (hemeralopia). Ackroyd[2] described cases of night blindness occurring in patients who were on inadequate vitamin A diets and who were exposed to bright lights. Such light exhausts visual purple normally but it is constantly regenerated. Ackroyd's cases did not regenerate their visual purple and night blindness resulted. It is believed therefore that vitamin A, normally found in the retina, is concerned with the metabolism of visual purple. Night

[1] The Vitamins, Mead Johnson & Co., Evansville, Ind., 1932.
[2] Ackroyd, W. R. Trans. Ophth. Soc. United Kingdom, 50, 230, 1930.

blindness is not uncommon in Far Eastern tropical countries where all forms of avitaminoses are abundant.

For some years vitamin A has been implicated in the etiology of urinary calculi and as a possible factor in sterility. There is a tendency at present to account for this on the same basis as the above, that is, an abnormal condition of the mucous membrane of the urinary tract favoring the formation of concretions, and of the genital tract in the female which prevents proper implantation of the ovum and its subsequent retention in the uterus. In the male, the same changes may produce sterility. The keratinization of the genital tract in the female results in such characteristic changes in the vaginal smear that observation of this change is in use as a method of vitamin A assay in animals.

Wolbach and Howe[1] have brought out evidence that vitamin A deficiency results in atrophy of the ameloblasts and odontoblasts in rats and guinea-pigs and Boyle[2] noted tooth hypoplasia in an infant on a vitamin A deficient diet.

In 1930, Mellanby[3] published an opinion that a deficiency in vitamin A may be a possible explanation of the subacute combined degeneration of the cord which occurred in animals on controlled defective intake of this vitamin. He suggested that the same state may underlie the similar degenerations in man seen in ergotism, pellagra, lathyrism and disseminated sclerosis. Acting on his own suggestion Mellanby has treated cases of early disseminated sclerosis with dietary measures and obtained highly satisfactory results.

All of the conditions cited above are relatively far-advanced results of vitamin A deficiency, or of this defect combined with some other factor such as a toxin. Although the storage capacity of the body for vitamin A is not great the clinical incidence of avitaminosis A is also not high. One assumption from this may be that the average diet contains an adequate amount of vitamin A to prevent these outstanding manifestations.

There remain therefore two further possibilities concerning vitamin A deficiency, (1) that there are intermediate states of ill-health due to relative deficiencies of vitamin A and (2) that the average state of health is not the optimum state that could be obtained on a vitamin A-rich diet. Little is known about these two possibilities at present but a prediction may be hazarded that those individuals who partake of vitamin A in amounts above those whose intake is just adequate to prevent evidences of deficiency will enjoy a measurably better state of health.

Vitamin B (Vitamin B Complex).—The vitamin B complex considered as a whole is a water-soluble compound containing carbon,

[1] Wolbach, S. B., and Howe, P R. Am. Jour. Path, 9, 275, 1933
[2] Boyle, P. E.: Jour. Dent. Res, 13, 39, 1933.
[3] Mellanby, E.: Brit. Med Jour., 1, 677, 1930.

hydrogen, oxygen, nitrogen and sulphur. Owing to the transitory state of knowledge regarding the individual components of the complex it would mean nothing to discuss its chemical properties in further detail for each fraction possesses its own capacity to resist heat, acids and alkalies.

In the natural state the vitamin B fractions occur bound together in the complex. The dietary sources for vitamin B stand therefore, with some exceptions, for each member of the group. The most abundant single source of this vitamin is the wheat germ. Large amounts are found in yeast, but recent assays of this substance show a disconcerting lack of consistency of vitamin B content. One of the most widespread sources is in the pericarp of rice grains, that portion of the grain which is removed by milling. It is present in amounts sufficient to protect against deficiency in whole barley, whole wheat bread, corn, cottonseed meal, sprouted grains, milled oats, whole rye, wheat middlings, whole bran, kidney, liver, brain, fish roe, lemon, grapefruit, and orange juices, tomatoes (raw, canned or dried), alfalfa, beans, cabbage, carrots, cauliflower, dandelion greens, eggplant, lettuce, onion, parsnips, peas, white potatoes, spinach, swede, turnips, most nuts (except almonds, peanuts and pecans), and in milk, buttermilk and cream.

The amounts of each of the sub-members of the group in the above animal and vegetable sources is variable and some foods are better sources of some of the fractions than others. Thus corn, or maize is listed as satisfactory for vitamin B as a whole, but is considered lacking in the fraction assumed responsible for protection against pellagra.

No precursor or provitamin for vitamin B has been demonstrated. It is believed that its synthesis by plants is complete and that no further conversion occurs before it is used in the animal body.

Due to its complexity in structure and use, vitamin B complex requirements must vary considerably under changing conditions of the organism. For the maintenance of health under normal conditions it may some day be possible to calculate the necessary daily intake but this cannot be done at present.

Lactation is believed to create a demand for higher vitamin B intake, and there is some indication that the requirement increases progressively during the periods of active growth. Correlations between caloric intake, proportion of carbohydrate in the diet, and protein consumption have been suggested but not generally accepted. It has been believed for many years, on a clinical basis, that heavy rice eaters show some such correlation between the high carbohydrate diet and development of beri-beri apart from the fact that they are using milled rice.

Accepting present knowledge of the individual factors of vitamin

B complex as incomplete, the following discussions represent the current opinions on this constantly changing subject.

Vitamin B_1 ("Anti-neuritic vitamin" of Eijkman and Peters, "Anti-Beri-beri vitamin," Vitamin F of Sherman).—Crystalline preparations from yeast which are believed to be nearly pure forms of this vitamin have been obtained by several investigators.

The formula for vitamin B_1 by Windaus *et al* is $C_{12}H_{16}ON_4S$. This has been confirmed by others. Kinnersley, O'Brien and Peters[1] believe that the variable physiologic activities shown by different crystalline preparations is evidence that these substances are still impure. Vitamin B_1 is unstable to alkali, relatively stable to acid and stable to dry heat. It is unaffected by a dry temperature of 100° C for twenty-four hours but is destroyed rapidly in the presence of moisture.

Seidell[2] states that samples "of dried brewers' yeast may vary as much as ten-fold in activity."

Sherman has shown that the vitamin B_1 content of milk can be diminished by feeding cows on a ration deficient in this vitamin. That 25 per cent of the vitamin B_1 of milk is destroyed by pasteurization has been demonstrated by Krauss, Erb, and Washburn.[3]

The physiologic effects of vitamin B_1 deficiency are largely manifested through the nervous system. Animal experimentation and *in vitro* studies have demonstrated that the action of vitamin B_1 is *concerned in the metabolism of nerve tissue and nervous response* mechanisms. (The anti-polyneuritis effect on fowl was one of the first evidences of the existence of the accessory food substances.)

The most general statement that can be made about the mode of action of vitamin B_1 is that it is involved in the oxidative processes of carbohydrate metabolism. This activity is possibly of the *nature of a co-enzyme effect; the enyzme suspected is probably that* of a dehydrogenase system.

Another evidence of its function is found in the consistent loss of appetite accompanying vitamin B_1 deficiency in animals and so conspicuous in the human vitamin B_1 deficiency disease, beri-beri.

The dilatation of the heart and disturbed heart-rate, which are *cardinal findings in human beri-beri are attributable to the influence* of the vitamin on nerve ending effects and local carbohydrate metabolism disturbances. Clinical vitamin B_1 deficiency is rare in the adult but not uncommon in infants of communities where the vitamin B complex deficiencies are most abundant.

As a factor in human disease the absence of vitamin B_1 is held *responsible not only for the cause* of beri-beri but for other sub-

[1] Kinnersley, H. W., O'Brien, J. R., and Peters, R. A.: Biochem. Jour., 29, 2369, 1935.

[2] Seidell, A., and Smith, M. I.: Jour. Am. Chem. Soc., 55, 3380, 1933.

[3] Krauss, W. E., Erb, J. H., and Washburn, R. G.: Ohio Agric. Exp. Sta. Bull., 518, 3, 1933.

clinical unhealthy states. The evidences for these latter are the otherwise unexplained dropsies or localized edemas common in tropical countries, disturbances of appetite and digestion from unknown causes, and failure to gain in weight by children on otherwise adequate diets. The neuritis of chronic alcoholism has been attributed to disturbed utilization of vitamin B_1, brought about primarily by the effect of alcoholism on the functions of the gastro-intestinal tract.

Vitamin B_2 ("Anti-dermatitis or Anti-pellagra factor" of Goldberger, P.-P. factor of Goldberger, Vitamin G of Sherman).—The major part of the fraction of vitamin B complex has been shown by György, Kuhn, and Wagner-Jauregg[1] to be chemically and actually identical with lacto-flavine the water-soluble pigment of milk. Vitamin B_2 activity and lacto-flavine are destroyed by blue or visible violet light, possess the same crystalline form and elementary chemical analysis ($C_{17}H_{20}N_4O_6$), and have the same absorption spectrum. Vitamin B_2 has been synthesized artificially. It is stable to acids, moderately stable to alkali, and is thermostable in neutral solution.

The principal food sources of this vitamin are milk, egg, muscle-meat, liver, yeast, wheat germ, peas, whole maize and maize endosperm.

In determining the vitamin B_2 efficiency of any food or preparation, the test rat is placed on a vitamin B_1-sufficient, vitamin B_2-defective diet for three to four weeks. Addition of the test material is then made to this diet. The vitamin B_2 unit is the amount required to produce an average gain of 3 grams weekly per animal for a period of eight weeks under the standard dietary conditions.

It is found that a diet including as much as 50 per cent of any of the cereals will supply enough vitamin B_2 for approximately normal growth.

Little is known about the physiologic activity of vitamin B_2. An interesting correlation has been found between flavine and Warburg and Christian's "yellow oxidation enzyme." This enzyme is now shown to be a colloidal enzyme fraction combined with flavine. Flavine can therefore be said to exist in free and combined forms. It is apparently necessary for the formation of the complex yellow oxidation enzyme which the animal organism cannot synthetize.

Harris[2] suggests that the most convincing evidence of a probable identity between flavine and the vitamin B_2 anti-pellagra fraction (P.-P. factor) is the fact that flavine is destroyed by irradiation and that a pellagra-preventive diet is rendered dermatitis-producing by similar treatment. He points to the seasonal incidence of photo-

[1] Gyorgy, Kuhn, and Wagner-Jauregg: Klin. Wchnschr., 12, 1241, 1933. Naturwissenschaften, 21, 560, 1933

[2] Harris, Lester J.: Vitamins, Ann. Rev. Biochem., 3, 278, 1934.

sensitization in pellagra as a possible effect of solar radiation on natural food materials or *in vivo* on subjects exposed to it.

The results of experimentation indicate that the effect of avitaminosis B, formerly attributed to B_2 as regards the formation of pellagra-like conditions is concerned, is due to deficiency of B_6 and that B_2 deficiency is not known in man. B_2 avitaminosis in animals produces loss of weight and eye lesions. Current opinion is strongly in favor of pellagra being due to a deficiency of vitamin B_6.

Vitamin B_2 is also implicated in lactation, promotion of growth, and hematopoiesis but clinical and experimental work on these possibilities lack confirmation necessary for more than theoretical consideration.

Vitamin B_3.—The existence of this vitamin is doubted. If it exists as an entity it is probably only of significance to lower animals. It has been termed the "third pigeon factor" by Williams and Waterman who claim that it is necessary for growth in these animals.

Vitamin B_4 (Reader's Vitamin).—The belief in vitamin B_4 has resolved itself into Harris'[1] opinion that "vitamin B_4 deficiency seems to resemble a state of chronic or persistent deficiency of vitamin B_1 since it can always be cured by the administration of a sufficiently large dose of vitamin B_1."

Vitamin B_6 (Anti-dermatitis Factor; Vitamin G).—The former vitamin B_2 has been broken down into vitamin B_2 and another fraction designated as B_6. It is believed that this latter may be one of several anti-dermatitis factors some one or more of which may be the pellagra-preventing vitamin.

The richest source of vitamin B_6 found by György[2] is fish muscle (herring, salmon and haddock).

Vitamin B_6 is inactivated by visible light. Its chemical composition is not known.

Vitamin C (Anti-scorbutic Vitamin).—Vitamin C is ascorbic acid. This is a water-soluble crystalline substance of known chemical structure (formerly known as hexuronic acid) which has recently been synthesized (Reichstein, Grüssner, and Oppenauer[3]). It is highly heat stable under conditions in which possibilities of oxidation are prevented. This is of great bearing on the preservation of the activity of vitamin C during the preparation of food, especially by canning processes.

It has been shown that canning of different foods requires individual consideration be given to the amount of ascorbic acid present, the pH of the food medium, the amount of moisture and the time required in the process. Anaërobic conditions are generally approached as far as may be required and when the process is one of

[1] Harris, L. J.: Ann. Rev. Biochem., 4, 346, 1935.
[2] György, P.: Biochem Jour., 29, 760, 1935.
[3] Reichstein, S., Grüssner, A., and Oppenauer, R.: Nature, 132, 280, 1933.

drying it is ordinarily carried out rapidly under pressure. The activity of vitamin C is not affected by high acidity in preserved fruit juices. Copper utensils favor inactivation of vitamin C and it is adversely affected by ultra-violet light.

Vitamin C occurs most abundantly in the following foods: tomatoes, oranges, lemons, raspberries, sprouted grains, raw cabbage, lettuce, rutabaga and swede. It is present in smaller amount in grapefruit, orange peel, string-beans, onions, peas, malt and white potatoes, and in variable quantity in cow's milk in proportion to its presence in the food ration.

Ascorbic acid is found in high concentration in the suprarenal cortex and medulla, and in corpus luteum.

There is no evidence of storage capacity in the body for vitamin C. Although evidence is accumulating that there is a parallelism between the ascorbic acid content of foods as determined chemically and their anti-scorbutic effect this knowledge has not been put into general application. It is expected that tissue assays and determinations of capillary permeability may lead to an index of vitamin C requirements in health and disease.

Ascorbic acid in the dose of 0.5 mg. per day has been found sufficient to prevent vitamin C deficiency in guinea-pigs.

The unit for vitamin C is the activity of 0.1 cc. of fresh juice of the lemon, *Citrus limonum.*

The essential rôle of vitamin C in the body is believed to be that of an oxygen carrier. It is able to perform this function by virtue of its power of reversible oxidation. On this basis ascorbic acid is looked upon as a promotor of oxidative systems in the tissues. That this is highly probable is shown by Euler and Klussmann[1] who have demonstrated that scorbutic tissues have low oxygen capacities which can be restored by the addition of ascorbic acid.

The outstanding clinical effect of a deficiency of vitamin C in man is the production of scurvy. This condition is too well known to necessitate a description of its pathology and symptoms. Evidence is accumulating however to show that there are many persons, especially children, who are in a sub-scorbutic state. This is manifested by studies on capillary permeability, which according to Wolbach[2] is due to a failure to form functionally perfect intercellular substances. The same investigator, with Howe[2] noted a similar deficiency in the ability of the body to form cementing substances in the teeth. This latter observation has received some degree of confirmation by Hanke[3] in his statistical studies on children in

[1] Euler, H., von, and Klussmann, E.: Zeitschr. f. Physiol Chem., 219, 215, 1933.
[2] Wolbach, S. B., and Howe, P. R.: Arch. Path and Lab Med, 1, 1, 1926
[3] Hanke, M T · Diet and Dental Health, Chicago, The University of Chicago Press, 1933.

Chicago who were treated with large doses of orange juice in an attempt to control gingivitis and dental caries.

Of special interest to clinicians is the frequent observation of peptic ulcers which develop in guinea-pigs on partial vitamin C deficient diets. Whether this has any bearing on the human ulcer problem is not known.

Vitamin D (Anti-rachitic Vitamin).—Through the combined investigations of Steenbock and Rosenheim and Webster[1] it has been determined that vitamin D is a sterol with the formula $C_{27}H_{42}O$ formed from another sterol (ergosterol), by the action of ultraviolet light. Ergosterol is therefore looked upon as the precursor *of vitamin D. In man ergosterol is found in association with cholesterol* in many tissues, especially the skin. The ergosterol of the skin is converted by the direct action of the ultra-violet rays in sunlight. In the laboratory, ergosterol may be converted by low voltage *x*-rays, the slow discharge, and radium emanation but much less effectively than by filtered mercury vapor lamp light.

The two most potent artificial preparations of vitamin D are vitamin D_2 of Windaus *et al.*, 42,000 International anti-rachitic units and Calciferol of Askew *et al.* with a potency of 40,000 I. A-r. units. *These are both in purified crystalline form.*

It is not at all certain that ergosterol in nature may not exist in several forms. Serious discrepancies have been noted between the anti-rachitic effect after irradiation of quantitatively determined equal amounts of ergosterol from several sources. It is probable that the active substance obtained by irradiation of ergosterol is only one of many of its stereo-isomers, and that ergosterol is not the only precursor of vitamin D.

The human does not synthesize ergosterol but obtains it from animal and vegetable sources, the most abundant supply being obtained from cod-liver oil, halibut-liver oil, turbot-liver oil, egg-yolk, whole egg, milk, butter, lettuce, yeast, and many cereals. It is found constantly in association with fats.

Vitamin D is exceedingly stable to oxidation and heating and for all practical purposes commercial and domestic methods of food preparation do not reduce its activity.

The International Unit of vitamin D is 1 mg. of a standard solution of irradiated ergosterol.

As with other vitamins, the amount of vitamin D in animal foods is influenced by the food sources of these animals. Thus wide differences in the ergosterol content of cod-livers has been found in cod from different geographic locations. Seasonal supplies of vegetable ergosterol are variable and as a result the vitamin D of *milk fluctuates with this change. The vitamin D content of eggs* can be increased by irradiation of hens.

[1] Rosenheim and Webster: Biochem. Jour., 20, 537, 1926; Ibid., 21, 389, 1927.

The ergosterol from the food is absorbed from the intestine and deposited in the tissues of man, largely in the skin. It is an example of storage by segregation. On demand, and following irradiation by penetrating ultra-violet rays, the activated ergosterol is absorbed into the circulation and distributed throughout the body. As far as has been determined it accumulates in certain areas, especially at points of bone formation and in the great arteries and kidneys. Although the exact mode of interplay between activated ergosterol and other body metabolites has not been determined there is sufficient evidence to say that it is connected with the absorption and utilization of calcium and phosphorus. Current indications are that vitamin D increases absorption of calcium and phosphorus, thereby raises the blood phosphate and/or calcium levels, and brings about indirectly an excess concentration of ionized calcium and phosphorus in those areas where the enzyme hexosephosphatase is most abundant. The action of this latter agent is to hydrolyze organic phosphorus compounds and cause a high solubility product between calcium and phosphorus (a local supersaturation), and the consequent deposition of calcium phosphate, $Ca_3(PO_4)_2$. The point of high concentration of the phosphatase being in the bones, it is obvious that the formation and deposit of calcium phosphate will be in these areas.

The sum total effect of vitamin D therefore is to conserve the net balance of phosphorus and calcium, that is, the difference between the amount of these minerals absorbed and the amount remobilized and tending to be excreted.

The increased acidity of the intestinal contents under the administration of vitamin D is believed by Drummond to be an indirect result of the metabolic activities just described and not from local effects on intestinal flora as postulated by others.

The connection between the rôle of the parathyroids and vitamin D in calcium metabolism has not been satisfactorily cleared up. Evidence that vitamin D stimulates the parathyroids or makes parathyroid secretions in the body more available has not been confirmed.

The foregoing effects on bone formation are characteristic of rickets and it has been definitely shown that rickets is a vitamin deficiency disease, especially avitaminosis D. Massive clinical tests and animal experimentation have amply confirmed this belief. Vitamin D is therefore called the anti-rachitic vitamin. The rôle of irradiation or ultra-violet light, in the prevention of rickets is now attributed entirely to its activating effect on ergosterol in the skin. Adult human skin contains 0.42 per cent ergosterol. There can be little doubt that ultra-violet light may penetrate the skin to depths sufficient to reach the stored ergosterol. That it acts on ergosterol in the blood of skin capillaries has been alleged but

not proven. It is more difficult for these light rays to penetrate dark pigmented skins thereby possibly accounting in part for the prevalence of rickets in negroes.

Categorically, vitamin D is a cause of rickets through its deficient intake, absorption or activation. Conversely, an adequate supply and proper utilization of this vitamin will prevent and cure rickets. The prophylactic dose is apparently much less than that of cure.

The supply of vitamin D may be augmented by increasing the quantity of vitamin D-containing foods, or by the administration of vitamin D concentrates. The effectiveness of the supply may be increased by artificial irradiation of food sources or of the body surface. Among the concentrates Calciferol and vitamin D_2 are the most potent (40,000 and 42,000 International Units per milligram respectively). Viosterol (irradiated ergosterol in vegetable oil) has a potency of 250 times the standard for cod-liver oil. The American Anti-rachitic Unit is that amount of vitamin D which when uniformly distributed into the standard vitamin D deficient diet ration (ration 2965, *Jour. Biol. Chem.*, **64**, 263, 1925), will produce a narrow and continuous line of calcium deposits in the metaphysis of the distal end of the radii and ulnæ of standard rachitic rats.

Accumulated trials of natural foods, augmented foods, and artificial concentrates of known vitamin D potency point to 1500 units daily as the average amount required for prevention of rickets and 3000 units for cure. Varying potency of natural and prepared sources makes it very difficult to determine accurate dosage in practice. Viosterol 250D is the best available preparation of vitamin D which is on the market. As a preventive of rickets it is given in the dose of 8 to 10 drops per day. One quart of milk (summer) contains, on an average, not more than 200 units, butter varies from 0.8 to 1 unit per gram, cod-liver oil 50 to 150 units per gram.

Vitamin D has been implicated in the production of dental caries but Klein and McCollom have brought forth evidence that deficient phosphate is of more importance in its production than a lack of the vitamin. The same observers link up the pathogenesis of pyorrhea with the same mineral deficiency.

Soon after the high potency vitamin D preparations were perfected reports began to accumulate of the harmful effects of alleged overdosage. The clinical and pathologic findings in this condition seemed to warrant the use of the term hypervitaminosis D but subsequent investigators have suggested that there may be some toxic agent in the materials used which causes the pathology. Harris and Moore[1] believe that their studies on foods and products of various potencies have shown that their alleged toxic effects were parallel to their vitamin D potencies and that the toxicity of preparations

[1] Harris, L. J., and Moore, T.: Jour. Biol. Chem., **23**, 261, 1929

of irradiated ergosterol is the same as their calciferol contents. Their conclusion is that vitamin D is itself toxic.

Vitamin D intoxication is an exaggeration of its physiologic action: blood calcium and phosphorus is raised and there is an over-deposit of bone salts at the epiphyses and an accumulation of calcium salts in other systems, especially the arteries. Calcium excretion shifts from the feces to the urine. General body tissue calcium may be greatly diminished. With these physiologic changes may go rapid loss in weight and more serious symptoms of a general nature with the possibility of a fatal outcome.

The amount of vitamin D necessary to bring about such serious results is from 25,000 to 50,000 times the minimum anti-rachitic dose. Nevertheless, the newer purified preparations containing 40,000 or more units per milligram are available and being put to greater use and so the danger of overdosage is not remote. It is unlikely that viosterol preparations could bring about harmful changes unless used with most reckless abandon.

Similar danger has been pointed to in the current custom of excessive exposure to sunlight on the assumption that the ultraviolet light will activate ergosterol in amounts far beyond the body needs and to an extent which may acutally be harmful. This fear may not be altogether unjustified where young infants are concerned and especially those who are on augmented vitamin D diets.

Vitamin E.—In 1922 Evans[1] reported the existence of a vitamin necessary for normal reproduction in rats and mice. In carefully controlled work on nutrition and the study of the estrous cycle, he and Bishop recognized the fact that the other vitamins, some of which were known to bear some relation to normal reproduction, could not be held accountable for the peculiarly characteristic forms of abnormal gestation in the female animals and the changes in the testes of males. To account for this they postulated a new vitamin which now bears the designation vitamin E, or the fertility vitamin (or antisterility vitamin).

Vitamin E concentrates show absorption bands in the ultraviolet which closely follow its biologic activity. The vitamin itself has not been isolated. It is fat soluble.

It occurs in Nature in the green vegetables and is especially abundant in lettuce, spinach, alfalfa and watercress. It is found only in the embryos of cereals. Smaller amounts are present in some of the vegetable oils.

In spite of its close connection with reproductive functions it is found only in minute quantities in the organs concerned. Its highest concentration in the animal body is in the fats and musculature.

[1] Evans, H. M.· Science, 56, 650, 1922.

Rats fed on vitamin E-free diets may not show the effect of withdrawal of the vitamin over as long a period as is required for the birth of four litters. This is given as evidence of an efficient storage mechanism.

Vitamin E deficiency in females results in a blasted embryo. Although the female is also believed to suffer from the lack in a more general manner it is the embryo which is mainly involved. Development of the embryo does not proceed beyond a certain point and is resorbed.

In the male, deficiency causes characteristic changes in the seminiferous tubules. There is degeneration of the epithelium until there is nothing left but the cells of Sertoli and the interestitial Leydig elements. The condition is progressive and irreversible.

There are no evidences of the presence or need of vitamin E in man and only preliminary indications that it may be necessary for rabbits, poultry, sheep and cattle.

Vitamin F.—See vitamin B_1.

Vitamin G.—See vitamin B_2.

CHAPTER XII.

THE DEFENSE AGAINST NUTRITIONAL DEFECTS.

DISTURBANCES of gastric and intestinal digestion, qualitative and quantitative dyspepsias, constipation, malnutritional states and the food excesses and deficiencies present *overwhelming testimony* of the ignorance of man as to what and how he should eat.

From all evidence the human instinct is poorly endowed with discrimination in the selection and use of proper food. Without this inborn capacity he is at the mercy of his immediately available food supply, race custom, training, propensity for imitation, acquired tastes, and his avid response to suggestion by his well meaning fellows, or the ulterior motives of commercial exploitation.

There is so much habit in race, national, community and personal customs of eating that the average individual denies any insinuation that he eats too well or too little or otherwise insults his digestive mechanisms. But it is the ease with which he takes up unconscious habits that makes the outlook hopeful for the inculcation of good habits without painful methods of reform. The intelligent guidance of infants, children and youths, without resort to methods which will make them dietetic hypochondriacs, should raise a generation of better eaters than their parents.

The metabolic processes of food digestion, absorption and utilization and the circumstances under which the nutritive elements are obtained and ingested can be the only accurate guides to proper diet and eating. Adherence to scientific selection of food does not preclude its esthetic preparation or the use of tasty condiments; on the contrary it encourages customs which enhance the attractiveness of food and makes eating a pleasure.

There is a basic dietetic requirement for every individual. Under the average conditions of an available varied dietary and the means to obtain it, it is assumed that this basic level is attained by the great majority of people. Although this may be true for most of the individual nutritive elements, a well filled stomach and a satisfied appetite cannot be cognizant of a defective supply of essential minerals and vitamins. Nor can the satisfied individual know that his diet is unbalanced or unfavorable in even more gross respects. For this reason it is necessary that he be given some measure of protection against his own inadequacies. Such protection can be given by the adoption of those community and individual measures that embrace the principles of prevention.

GENERAL PROTECTIVE MEASURES.

1. **On the Total Bulk for Community Needs.**—Few communities today can be independent in their food supply. Through the growth of highly urbanized areas there has developed a reduction of the facilities for a self-sufficient food supply. Rural communities have become more dependent on distant sources of food because of the rapid growth of the canning and preserving industries and the possibility of shipping perishable foods long distances by refrigeration.

As a consequence most people are partly or entirely at the mercy of commercial food supplies over which they have no control. Community authorities therefore must accept the responsibility of seeing that the total food raised in, or shipped into their territory is adequate. They must be prepared to meet emergency defects brought about by economic conditions, physical catastrophies, and significant changes in population.

Legislative measures and sanitary codes can do much to help the easy flow of bulk staple foods into and out of communities. Conversely restrictive regulations which do not give consideration to maintenance needs of the populace can do tremendous harm. There are abundant instances where such enactments have been made in the face of absolute food shortage in deprived communities. Constituted authorities can prevent the purposeful wastage of such supplies as milk and potatoes at any time, and especially when many of the underprivileged are experiencing an actual shortage.

Distribution of food to the necessitous is an acknowledged duty of organized communities either through official agencies or voluntary relief organizations.

Recognition of these principles by a community as a whole, can and will result in better community health if they are properly correlated with economic and social betterment.

Such blanket measures are conservators of human lives and efficiency and reflect on the health and prosperity of the community. In any civilized state there should be no widespread evidence of malnutrition in even the lower strata of society. The degree to which it is present can be taken as an index of the failure to apply intelligent action to a proven preventive principle.

2. **On the Quality and Quantity of Special Foods.**—The amount, variety and quality of individual foods may be affected by general measures. If it is known that any method of processing is injurious to the nutrient qualities of a food it may be regulated by law; if a monopoly exists in the distribution of an essential staple supply and this results in a serious inadequacy due either to unjustifiable price levels or partiality to geographic areas or social groups, restraining measures against it can be adopted. Unjust taxation or protective

tariffs may deprive a community of foods for which it is dependent on outside sources.

It is possible through education to improve the quality and quantity of farm and dairy products. In the United States this function is performed by the Department of Agriculture through pamphlets, lectures, radio talks and exhibits. The State Fair is an impetus to improvement in stock and food products. The amount of these general measures which may be required and the direction in which they should be employed, *can only be determined by accurate* knowledge of the nutritional health of the community and understanding of the factors involved in the nutrient value, optimum production, and intelligent distribution of food.

3. **On the Individual Nutritive Elements.**—**Water.**—One of the first concerns of a community is its supply of drinking water.

Every inhabitant requires drinking water and he makes positive that he gets it from his own stream, spring or well or by pooling his interests in communal projects. The communal system requires oversight and with this goes responsibility of regulation. On this basis have been built the systems of supply, from the small community well to the reservoirs that involve whole rivers and lakes under state and federal control. The maintenance of these water sources involves the assurance of an adequate per capita supply for drinking and other purposes without interruption. When this fails, water shortage reveals itself in the health of the populace.

The mechanisms of water metabolism reveal enough of the harmful consequences of prolonged, even partial insufficiency of this element, to necessitate efficient control over its supply.

Proteins.—Little can be done to influence the protein supply by general measures. Poultry, dairy products, animals and fish are the sources most commonly affected by controlling practices but the control is usually not motivated by consideration of their protein content. It is only indirectly that regulation of their supply or distribution influences this nutritive element. In some isolated communities the general protein supply may be limited to occasional game animals or fish. If, under these circumstances, prohibitions are placed on the capture of game a serious shortage might result.

Pellagra is a disease of defective nutrition closely concerned in the protein supply. There can be little doubt that in communities where pellagra is present, and in institutions, that those in authority can prevent the occurrence of this disease by seeing that the dietary contains adequate amounts of the required proteins. Various agencies can of course encourage the greater use of protein foods.

Carbohydrates.—The present tendency is more toward a per capita excess consumption of carbohydrates than toward reduction. The average yearly consumption of sugar per capita in the United States is 115 pounds, an increase of over 500 per cent in the last fifty years.

Candy sales have jumped enormously and the use of other forms of carbohydrate foods, such as corn syrup and bread show large increases. General measures against this unprecedented consumption must *reside in education. If the public health authorities shy from incurring* the disapproval of Chambers of Commerce, other agencies can *direct their propaganda against this harmful practice.*

Fats.—The control of fat consumption in any general way is almost entirely limited to Federal Regulations on the sale of butter substitutes and the fat content of milk. By maintaining the power of inspection through its Meat Inspection service of oleomargarine made from animal oils government can assure a known product for general consumption. It has no control however over oleomargarine made from vegetable sources. One of the measures of the nutritive value of milk is its fat content. In most communities a required percentage of fat in whole milk is fixed by law, and milk which has this percentage becomes the standard milk for sale in the community. The standard fat content of milk adopted by the United States Department of Agriculture is 3.25 per cent.

Although the purpose of setting a minimal amount of fat in milk is not entirely to insure a milk of specific nutritional value it does influence the quality of milk fat supplied to a community. Because of its nutritive value and vitamin content a high fat-content milk is a better milk. Children and infants fed and reared on cow's milk may suffer materially if the milk is persistently below standard requirements. In one foreign country the prevalence of xerophthalmia was taken to indicate that the milk supply, most of which was imported tinned milk, was inadequate in fat. On this observation alone the import standard was raised from 3.25 to 3.50 per cent. A high standard milk tends to encourage breeding of cows which will give high quality milk.

The various liver-oil preparations now marketed for their vitamin content are standardized in America under the Food and Drugs Act.

Mineral Elements.—When the relationship between endemic goiter and iodine was recognized various companies commercialized this knowledge *by integrating iodine salts in their products.* Table salt was the most popular. In some localities government regula*tions were made requiring all table salt sold to contain a measured* amount of iodine. Subsequently, it has been found that iodides *in salt deteriorate and so lose their effectiveness. Furthermore,* it was soon realized that the indiscriminate use of iodide by the general population took no account of those hypersusceptible to it and those with thyrotoxicosis. As a result the more common practice at present is to permit the sale of both iodized and iodine-free table salt but to insist that those brands containing iodine be so labeled.

In some communities sodium iodide is added to the general water supply (Rochester, New York). Sodium iodide added in the amount of 0.664 pounds per 1,000,000 gallons results in 50 parts per 1,000,000,000 in the tap water delivered in the city of Rochester. This is 10 times the amount found normally in the city water.

If either of these measures prove practical and harmless they will undoubtedly diminish the incidence of endemic goiter in goitrous regions.

Municipal water plants generally carry out careful analyses of the mineral content of their water supply. The great number of commercial, household and personal uses to which water is put necessitates a knowledge of its mineral content under all of the conditions that cause it to vary, such as season, rainfall, dual sources and changes in catchment areas. Although the reasons for knowing the amount and kinds of minerals present are largely commercial and industrial, the hardness or softness of water has considerable influence on the health and cleanliness of the consumers. The laxative or constipating effect of a change of drinking water brought about by a change of residence is common observation. Beyond the possibilities of bacterial contamination of the water this influence is due almost entirely to the proportion and concentration of its dissolved minerals. The mineral salts mostly involved are calcium and magnesium, which predominate in hard water. Over long periods of time every individual consumes enough of these important elements to have an important bearing on his total intake of minerals. There is some evidence that populations living in areas in which the water contains a high percentage of calcium manifest a relatively high incidence of calcification of the arteries. It is evident that the importance of the water supply as a source of necessary mineral food elements will be inversely proportional to the availability and supply of these elements in other foods.

The mineral content of the water supply can be deliberately raised or lowered. Gross sediment can be removed by filtration and settling basins; very fine suspended particles must be coagulated or precipitated. For the latter, aluminum sulphate (alum) or sulphate of iron are used. Hard water may be softened by the use of lime and soda ash, permutit, distillation or condensation.

Additional emphasis on the need of better understanding of the effects of dissolved minerals on the health of the consumers is given by the recent revelation that "spotted enamel" of the teeth is caused by a high fluorine content of the drinking water.

Much remains to be known about the importance of the mineral salts in water to the disease conditions in which they are concerned, but should present suspicions be verified, the control of the mineral content at the water source or before it reaches the consumers, should be beneficial.

4. **On Group Food Habits.**—The individuality of communities, nations and races in respect to their food habits is a subject of common remark. Thus, a locality may have a reputation for a self-imposed monotonous dietary; a nation may be known as addicted to food excesses or the subject of specific deprivations; or a race may have its customs of eating restricted by prohibitions. As a result all individuals of these groups are consciously or subconsciously the subjects of the group habits and customs. Infants and children cannot choose their food but have it provided for them under the selective control of their adult guardians who were brought up under the same circumstances. If there are any harmful elements in the quality or quantity of food provided, they are perpetuated through this cycle of impressed habits. A few examples of the better known group habits may be cited: the predominance of hominy, corn and beans in the southern part of the United States; the peppered dishes of Mexico; the high sugar and white-bread consumption in the United States; the heavy meat and potato meals of the English; the elaborate cuisine of the French; the predominately rice diet of the Orient; the Hindu restrictions on meat and the limitations of the Jews to kosher food. It is not argued that all of these are essentially harmful but that in the absence of other supplemental foods or qualifying circumstances they may be so. Unfortunately many of these customs are grounded in economics. The diet of many communities in the southern part of the United States, which is so conducive to the development of pellagra, is largely necessitated by the inability to obtain a balanced diet.

Harris[1] speaks of "Sugar-saturated, vitamin-starved America." This is an indictment of the American public on its unintelligent acquiescence to the pressure of commercial enterprises which have succeeded, in the space of a few decades in imposing a whole new set of habits upon it. Advertising, makers of palatable and attractively attired sweets, food fad promotors, favored tariffs to traders in sugar, "health" drinks and sweetened beverage manufacturers, have all played their part in making America sugar-conscious.

The only reasonable defense against harmful group habits is education. Food acts and legislative measures against false claims in advertising, and adulteration of food, or possibly even the control of food faddists, can hardly be expected to be effective without the intelligent understanding of the people as to why such regulations are necessary.

Habits that are rooted in long-standing custom can only be uprooted by widespread instruction and the presentation of constructive substitutes that have specific appeal to local tastes. Where prejudice, superstition, or religious beliefs limit the diet in important

[1] *Harris, Seale Am. Med*, 34, 837, 1928

food elements no enactments by law, or moral reforms can hope for success in changing existing customs unless they work subtly to alter the conditions on which the customs are founded.

Child education is the most efficient field for intelligent reform. By teaching school children good habits of eating and the principles of dietetics while they are studying the graded courses of hygiene, a new generation of good eaters can be raised.

Social and economic reforms can bring about dietary changes in communities more rapidly than any other method. In a measure the people are bought off and embrace the changes in food along with the other changes.

Physicians should play a great part in the public instruction in this matter. They can fulfil this function through such agencies as parent-teacher groups, school boards, local clubs and institutions, published articles in lay magazines and the press, and their coöperation in every sound movement which aims to instruct, educate and advise groups of people as to how and what they should eat.

The physician in private practice is no less obligated to help spread the knowledge of good eating habits than the doctor occupying an official administrative position or in public health work; his circle of influence may be smaller but he is frequently in a position to be more impressive than the doctor speaking in his official capacity.

Industrial physicians and those connected with institutions must face the challenge of such conditions as pellagra, scurvy, and nutritional anemia, and should never allow them to appear in their charges. School board appointees or medical advisors should have a thorough understanding of the hygiene and growth requirements of children and should insist on their privilege of scrutinizing every proposal which may bear on these essentials.

Inestimable improvement should follow the application of blanket preventive measures against nutritional defects. Even with inadequate knowledge of many of the nutritional factors and ignorance of the mechanisms involved in the natural history of many suspected food-deficiency diseases there is hardly another line of prevention which can be more effective. Scurvy in the British Navy fell before the onslaughts of intelligent use of an empiric observation centuries before the discovery of vitamin C; rickets has all but disappeared in groups and localities where propaganda and control have established efficient diets and hygienic habits of living for their children.

It is not too prophetic to believe that the incidence of diabetes, pernicious anemia, sprue, pellagra and many forms of gastric and intestinal dysfunction can be reduced by continued efforts to understand their causative factors and the application of effective protective measures against them. With this should come a generally improved state of growth, development and radiant health in the general population.

PERSONAL PROPHYLAXIS.

The ideal diet is the physiologic diet. The ideal practices of eating are those based on physiologic principles. If causative factors other than those embraced under nutritive elements did not play a part in the maintenance of health and causation of disease it would be possible for any individual to be in perfect physiologic health by conforming strictly to physiologic requirements. But because other factors are involved this is an ideal never to be attained. The multiplicity of factors is the basis for saying "one man's meat is another man's poison." Diet is a strictly individual problem. Although any one individual may be heavily influenced by environmental circumstances which affect the nature of his food supply, what he likes, what he eats and what is "good" for him is his own personal concern. In the main therefore the individual, in full possession of his faculties and independent in his choice and use of food, is the final arbiter of his diet and habits of eating.

In the previous section it has been shown how the individual may be influenced by law, persuasion, suggestion and education. *Personal prophylaxis involves personal choice in so far as it can be* applied under the conditions set up by the environment; it is the *conscious or habitual application of known preventive efforts after* the operation of the general preventive measures have exerted their *effects.*

Individual Tastes for Food.—The infant, soon after weaning, exhibits likes and dislikes for certain foods. It is difficult to explain this on physiologic principles but relatively easy to trace the reasons to psychic factors. Careful observation of the food habits of a young child will generally reveal that a certain like or dislike for a food is based on such things as mimicry, association of the food with unpleasant experiences, injudicious force or persuasion, unesthetic preparation, punishment, misguided rewards and pampering, the influence of other associated habits and physical-mental states and the unintelligent assumption that a child can judge what it needs. On top of all these may be the ideas and prejudices of fanatic parents (and grandparents) about infant feeding.

Attempts have been made to determine whether man can select his food in response to physiologic demands. It is admitted offhand that water-lack produces its own needs and is interpreted as thirst and that the required bulk of food is met by appeasing hunger. It *is alleged that physiologic demands for salt operate in a subtle way* to see that enough of it is obtained and that if it is not in sufficient quantity in the diet it will be automatically sought for.

Clara Davis[1] has made an important contribution to the science of dietetics through her experimental studies on self-selection of

[1] Davis, Clara: Am. Jour. Dis. Child., 36, 651, 1928.

foods by infants and young children. She has shown that these children can and will select foods of varying quality and quantity and that this selection over a period of time will satisfy physiologic needs. However, their ranges of choice were not wide and the foods offered presented the possibilities for a balanced diet. There appears to be no evidence in her studies that there is any conscious or subconscious choice of materials which could be interpreted as an attempt to satisfy the requirements of individual food elements. The important part of Davis' work is the proof that children relish simple foods well prepared and served, even though offered with monotonous repetition; that food habits are extremely labile; that the alleged insults to digestion as practised by hungry children may be shocking to sophisticated appetites but, unless they are highly excessive, do not harm the children. It is assumed that the food offered is wholesome and intelligently selected and prepared.

The peculiarities of appetite in pregnancy can be put down to personal whims of unexplained origin, coupled with the general affections of the appetite common at this time. Although it is claimed that there is an alkali deficit in pregnancy there is no certainty that the tendency of pregnant women to indulge in base-forming foods can be called a physiologic response.

It has been said that Pica, or dirt-eating in children is an example of a habit growing out of a need—in this case calcium. Most pediatricians do not hold this view but point to the habit as a distinct perversion which manifests itself most commonly in mental defectives, and that it bears no relationship to calcium needs although the latter may be co-existent with it.

On the whole there does not appear to be any well-founded example of the selection of a food for the filling of a specific physiologic need.

The factors common to the formation of most habits and customs seem to be the only explanation for the choice of food in health. Where the refusal to eat an article of food is not based on idiosyncrasy to it or actual indigestibility, a harmful deficit of some one or more important food elements may result. A child who can take milk without suffering from hypersensitive reactions but will not drink it because it doesn't like it, is handicapped in its optimum nutrition. The same is true of eggs, many vegetables, and in some children, even of meats and fruits. These few examples indicate the possibilities of vitamin and mineral inadequacies that may result from persistent dislikes.

Adult habits may be no less harmful than children's. It is not uncommon to find people who believe that they cannot eat certain meats, fried foods, milk, eggs and other staple foods even though there are no signs of idiosyncrasy or derangements of digestion other than those brought about by their harmful habits of eating. These

habits are frequently the rationalized results of faulty training in childhood.

There is a further tendency to limit the dietary with increasing age. The author is familiar with an elderly lady of high social position who developed pellagra because of her peculiarly limited monotonous diet.

The problem of personal prophylaxis against qualitative defects in the choice of food resolves itself largely into one of inculcating broad likes for food in childhood. On the basis of Davis' observations and many examples in common experience it can be said that infants and young children can learn to like anything. Some of the most distasteful dishes to the adult palate are eaten with relish by children.

It is most important therefore to serve children well, to give them a moderately variable diet but not all of the highly specialized dishes of the adult table, to take into account every recognizable psychic factor which might influence their taste for a food, and to regulate other habits which might have a bearing on their manners and customs of eating.

The adult must be informed of the foolishness of his whims and shown the possibilities for harm in his senseless habit. Success in bringing about a change of habit requires education in physiology and dietetics in order that there may be a permanent intelligent base for the new conviction.

Digestibility and Compatability of Foods.—Most foods ordinarily eaten by man are readily digested and can be taken in endless combination without harm. What is interpreted as indigestibility is more often faulty digestion unconnected with the kind of food eaten and due to other causes, or it is a gastro-intestinal disturbance brought about by bad food such as infected meat, sea-food, milk products, etc.

Lean meat and meat well-done are equally digestible when considered in terms of the ability of the digestive ferments to reduce them to their end-products. The digestion of the proteins in an ordinary meal is according to Atwater[1] 92 per cent complete. Hawk and his co-workers have made exhaustive studies on the digestibility of all varieties of foods and there is nothing in their findings that would indicate that any of the commonly used animal protein foods are indigestible. Furthermore the relative digestibility of different animal foods, if measured by the time that they remain in the stomach, show such slight differences that they may be considered equally digestible. Sea-foods are as digestible as meats.

When proteins are taken in large amounts there is a tendency for them to remain longer in the stomach and if the intake is exces-

[1] Atwater, W. A.: Farmer's Bull. 142, U. S. Dept Agric, p 24, 1902.

sive it may readily lead to a sense of fulness and discomfort. It is probably for this reason that cheese is considered indigestible, it is generally eaten at the end of a meal which has itself produced a feeling of satiation.

Boiled milk is more rapidly emptied from the stomach than raw milk and milk drunk rapidly is more readily digested than milk which is taken in sips. Whole milk is passed out of the stomach more quickly than skimmed milk. These differences in milk are largely due to the size and consistency of the curds. Boiled milk curds are small and flaky and skimmed milk curds are large and tough. Milk taken rapidly forms smaller curds than sipped milk.

Eggs prepared in different ways also show tendencies to vary in the length of time they remain in the stomach. Raw white of egg is the most rapidly evacuated; raw yolk and raw whole egg show more delay than raw white alone; hard boiled eggs remain longer than soft boiled, and poached and fried eggs are equally as digestible as boiled eggs.

Of the vegetables it may be said in general that the higher the protein content and the smaller the undigested residue the longer they remain in the stomach. On this basis beans are more slowly evacuated than other vegetables and the leafy green vegetables leave the stomach more rapidly than potatoes.

Pastries are no more indigestible in themselves than any other foods. It is only when they contain large amounts of sugar or fats that their emptying time is delayed.

Fat foods are generally slowly evacuated but this is modified in part by the extent to which the fat is incorporated in the foods. When pastry is fried in deep fat the cooking coats the pastry base with a layer of fat, and it leaves the stomach more rapidly than when the fat permeates the pastry as in slow cooking.

Sugar in tea and coffee and the fat in cocoa delay the emptying time of these foods. Concentrated sugar, whether in solution or solid form is handled slowly by the stomach. Sweet potatoes remain longer in the stomach than plain white potatoes.

It is quite obvious that side from thoroughness of cooking, which in itself favors digestion, the apparent digestibility of foods is greatly dependent on the bulk of food in the stomach and the length of time that it remains there. Furthermore, the addition of slowly digested foods to a meal that would otherwise be rapidly digested will accentuate the belief that the foods are incompatible.

If carbohydrates remain too long in the stomach they undergo fermentation so that in addition to the stomach contractions against the bulk of food, there may be added gaseous distention. Such discomfort may very readily be misinterpreted as due to some one or more indigestible foods in the meal.

Rehfuss[1] has recently shown that the belief in the incompatibility of protein and carbohydrates taken in the same meal is entirely erroneous. Moreover it is an impossibility to prepare a meal of common foods without a mixture of these two food elements since all animal foods have some carbohydrate in them.

Continued lack of respect for the above observations can readily lead to chronic forms of indigestion. Although the stomach can deal with almost any type of food singly and most types in reasonable combinations, it can be embarrassed by surfeits of proteins, carbohydrates or fats. Disturbances of the motility of the stomach and intestinal tract resulting from altered balances of the mechanisms of peristalsis may produce the common functional dyspepsias.

McLester[2] points out that the order in which the foodstuffs are taken in the occidental menu is in good correspondence with the satiety values of the foods. The opening course of soup with meat extracts calls forth gastric secretory activity by direct chemical action and by psychic response. The entrées and main meat course, largely protein, have a high satiety value which is proportional to the amount eaten. Vegetables containing starch add to the satiety already begun. Salads with oil dressings cause the foods to remain longer in the stomach and intestines, and the sweet dessert enhances this still further.

Meals and Eating.—Hunger is the fundamental factor underlying the number of meals taken in a day and the way in which they are spaced. Some of the other factors concerned are age, habit, economic status, opportunity or lack of opportunity to stop for a meal, psychic attitudes toward food and the presence of some underlying physical condition which increases or decreases appetite or digestion. It can hardly be said that there is any definite or normal number of meals to be taken in twenty-four hours. Enough has been revealed in the previous sections of this chapter to show that habit, tastes, physiologic needs and kinds of food may all modify a person's appetite and the satisfactions obtained from eating.

Physiologically, the stomach requires a number of hours or minutes to empty itself of a given food. If any one or a combination of foods has given satisfaction by removing hunger there can be little physiologic demand to continue eating. Conversely, when the feeling of satiety has passed off the processes of hunger will begin again, and demand more satisfaction. Such a cycle would be entirely physiologic in a person who is free of undesirable psychic attitudes toward foods, whose habits of eating are of minimal importance to him, and who has no disease conditions which would create abnormal reactions to food. He would probably eat only

[1] Rehfuss, M. E.: Jour. Am Med. Assn , 103, 1600, (November 24) 1934.

[2] McLester, J. S : Nutrition and Diet in Health and Disease, Philadelphia, W. B. Saunders Company, p. 140, 1931.

when he was hungry and only as much as he would need to satisfy it. This manner of eating would not necessarily assure him an adequate diet but would probably result in a sufficient bulk and caloric intake. The diet of the infant is of this nature. Milk has a satiety value for the infant but it is not of long duration. Experience of the race and the demands of the infant cause the mother to nurse the child at frequent intervals. Pediatricians formalize this hunger cycle by instituting regular feeding hours thereby anticipating distressing hunger and inaugurating physiologic rhythm. These two, with good quality milk and adequate quantities of it at each feeding, meet all of the infant's physiologic demands and train digestive responses.

In the older infant the same principles are applied to a more complex dietary and this is kept up in childhood as long as it can be made compatible with increasing emotional attitudes toward food and rapidly developing habits of eating. In the average adult the underlying physiologic demands are almost unrecognizable beneath his complex habits.

The adult has just as many physiologic needs as the infant but because his greater freedom of action lets him eat when and as he pleases it becomes possible for him to enjoy a higher degree of flexibility in his dietetic habits.

With the exception of the long interval during sleep, the time between meals for the adult averages about six hours. It may be that three meals of high nutritive and satiety value in twenty-four hours is the physiologic optimum for the human. The morning meal may be early or late in relation to the beginning of the day and the midday meal may be taken when opportunity permits but the average person usually partakes of both. The evening meal is generally the formal meal and the one most likely to be complete. Reversal of the meals is commonly seen, some eating large breakfasts and small suppers, and others dining most heavily at midday, but on the average the meals are spaced about six hours apart.

The final judgment of the individual as to the proper time for his meals and the amount to be taken at each should depend on the satisfaction of three requirements: that the total quantity in twenty-four hours shall meet the caloric needs; that enough of all nutritive elements to prevent deficiencies are supplied *in the total foods* taken over a given period of time; and that the intervals between meals are not so short as to cause overloading of the stomach and intestines, or so long as to create harmful physical and mental responses to hunger.

Eating between meals is not harmful *per se,* but all individuals cannot indulge themselves outside of meal times without interfering with their appetite or digestion. Children cannot judge whether or not a sweet taken before dinner will interfere with their appetite.

But common experience shows that candies and sweetened beverages taken soon before dinner do interfere with the appetite of the majority of children and it is generally considered to be a harmful habit. This probably is a fact. On the other hand there is no evidence that a few sweets well spaced between meals are harmful. There can be little doubt that if the child's morning meal could be less hurriedly eaten and the school luncheon more intelligently planned much of the difficulty of the extra sweets problem would be removed.

The adult habitual between-meals eater is generally a poor regular meal eater. This is excepting the heavy worker who finds it difficult to satisfy his appetite at meal time. Nor does it include the common use of the late night supper following a long evening.

On the whole, regular hours of eating are more conducive of good digestive health than irregular meals. There is a degree of education in the digestive processes and the upsets which result from a change from regular to irregular meals is due as much to disturbance of trained rhythmic responses to food as to the psychic attitudes brought about by the new regimen.

Since the discovery of the conditioned reflex by Pavlov much has been written about the psychic response to food. It is urged that we come to the meal in a happy, congenial frame of mind and refrain from becoming angry or emotional while eating.

The person who is in a poor mood to eat generally eats poorly. There may be less gastric secretion, and pancreatic and intestinal stimulation as a result of his unappetizing attitude toward food but what is equally important, he eats too little and selects his food poorly, or eats too rapidly.

On the other hand when every one is happy and care-free around the table it is no assurance that the digestion of the meal will be as pleasant as the occasion. Overeating and poor judgment in the number and variety of helpings is as common at the congenial board as at the table of the psychically upset.

The symptom complex that follows a meal taken under mental stress is called nervous indigestion. The experience of this condition is so universal that the relation of cause and effect is unquestioned. If the mental perturbation cannot be avoided it is best to eat a little of the simpler foods offered and hope to supplement the meal later.

One of the most important mechanisms of eating is the mastication of food. Muscle fibers, starchy foods and green vegetables are more readily reached by the digestive juices when they are in the comminuted state. This results in more rapid and complete digestion and less delay in the stomach, both of which are important in preventing overloading of the gastro-intestinal tract and incomplete digestion with consequent undesirable fermentation and putrefaction. Poor mastication generally means that the food is bolted

and this is often accompanied by the swallowing of air (aërophagia). It is generally believed that swallowed air is a more frequent cause of distention of the stomach and belching than the gases produced by fermentation. Overemphasis on mastication is as harmful as underchewing. The retention of food in the mouth for a long time just in order to chew it creates in itself a morbid attitude toward food. As a result less food is eaten, and there are frequently distressing consequences, such as loss of appetite early in the meal, dysphagia through fear that the food may not have been thoroughly chewed, and gastric neurosis from the belief that any visceral sensations which might be felt are due to faulty organic indigestion. Fletcherites embrace the cult largely because they are of the type who are already over food-conscious.

General bodily fatigue depresses digestive functions and if food is offered to the stomach at this time digestion will be interfered with. For this reason it is best, when overtired, to rest before a heavy meal or to take small amounts of plain food.

THE PHYSIOLOGIC DIET AND FOOD HABITS.

The most fundamental function of all organisms is the acquisition of nutrient from its environment. It must show selectivity in its choice of foods whether this be by simple reflex response as in lower forms of life, or by intelligent judgment. In order that growth, development and repair may be possible all essential food elements must be available and in a form that can be utilized, and for a continued state of health they must be assimilated and metabolized by mechanisms which are in the condition to dispose of them without becoming harmfully unbalanced. If all of these conditions are satisfied the organism is in a state of nutritional health.

The physiologic diet therefore is one which supplies the elemental food principles in useful forms and amounts, and physiologic food habits are those which comply with the physiologic limitations of the mechanisms of assimilation and metabolism.

Current investigations in nutrition continue to add so much to the knowledge of the importance of the "little things in diet" that it cannot longer be taken for granted that alleged normal diets are optimal diets. While the average dietary of a well supplied and regulated population may contain enough of the essential food elements for growth and life itself there is no assurance that the individuals are receiving these elements in the best possible amounts and forms.

Unfortunately, most people are satisfied with average nutritional health. Until education can overcome this complaisance toward less than the best, it devolves on those in authority and who know the facts to see that the others are protected from their ignorance.

All of the blanket measures against defects of nutritive elements have this as their aim.

There can be little excuse for failing to apply known preventive *principles in dietetics. Although the number of known nutritive* elements may be increasing they are all available in common foods. Even with the addition of the vitamins, minerals, and salts to the list of necessary food elements there has not been a single "new" food added to the diet. All of these newly discovered or recently appreciated substances have either been available or already in use for a long time. What has now become necessary is the establishment of mechanisms that will insure an equal spread of the staple foods containing all of the essentials, to all classes and ages, irrespective of whether they have the intelligence to understand the reasons for their use or the will to use them.

The term "balanced diet" is becoming a popular phrase. If this is not to become just another fad in the minds of the unthinking, something must be done to see that the balanced diet becomes an unconscious habit. The only way this can be done is to see that the materials to balance the diet are available to all at reasonable prices. This means simple foods and fortunately again it is the simple foods which contain all that is needed.

All of the basic requirements for an adult daily diet will be met by one kind of meat, 2 eggs, 2 cooked vegetables, 2 fresh vegetables or salad, some fruit or fruit juice, butter, whole wheat bread, and 1 pint of milk. The meat may be animal or fish protein; the eggs may be prepared in any manner desired or incorporated in puddings or custards; the vegetables can be starchy or green, but the two *should be varied from day to day to prevent monotomy; tomato* juice may be substituted for fruit juice; and rye bread can be used in place of whole wheat bread.

On this basic diet all desirable variations in the cuisine of the sophisticated table may be constructed. Because food appetizingly *prepared has a valuable psychic effect favorable to digestion it* should always be given consideration. This is especially true with finicky eaters who are poor eaters at best. Overstimulation of gastric response by excesses of highly seasoned condiments is a physiologic insult.

The carbohydrate content of the adequate diet is sufficient without the addition of crystal sugar. Artificial sweetening of food "at the table" is an acquired habit and if it is indulged in should be done with restraint.

The undigested component of the meat, vegetables, fruit and milk supplies enough roughage to stimulate the intestine, give bulk to feces and aid elimination. If laxatives are required on a basic diet it is because some element such as fat or carbohydrate has been taken in an amount not in keeping with the requirements.

Considerable stress is laid today on the acid and base-forming foods. In the basic diet the acid-forming meats will be outbalanced by the base-forming vegetables, fruits and milk, which is to be desired.

As a result of individual inability or unwillingness to correct faulty habits of eating and to select wholesome foods, digestive disturbances are the common lot of mankind. Self-correction of diets is generally unsatisfactory because the cause of the indigestion is misinterpreted and the corrective effort is wrongly directed. As a result the sufferer is open to suggestion from any source and this is too often as fallible as his own. He then becomes an easy prey to commercial exploitation, food cultists and the practical dietitians among his friends. It is unfortunate that so many of the food fads and advertisements contain so much truth, for in the case of nutrition, half truths are exceedingly dangerous. Fletcherism overdoes an important physiologic principle; vegetarianism limits the diet to these essential foods but a vegetarian diet can hardly be varied and complete enough to satisfy protein and fat requirements; fast days rest the stomach and encourage insults on the other days; fruit and nut diets can never in themselves satisfy body needs; internal bathing with massive volumes of water can do no good and has a deleterious effect on the activity of digestive secretions; reducing diets are too unintelligently arranged and applied to be effective without the danger of deficiencies of many kinds.

The best general advice for a health maintenance diet is to know broadly what the food essentials are and to make sure that they are all obtained. The soundest individual advice is to balance the quantity of foods first and then plan for variety, avoid all excesses, and eat regularly.

It is a false assumption that the cultivation of food-consciousness breeds hypochondriacs. It is the hypochondriacs who view food from the wrong angle.

It is probable that the present known rôle of nutritive elements in the etiology of disease is but a shadow of what is to come. Every phase of clinical medicine and every branch of the medical sciences is concerned with nutritive factors as causes of disease or as participants in important disease mechanisms. Wherever they have been so revealed a step has been taken toward the prevention of the conditions in which they are involved for "To obstruct or intercept a cause is to prevent or dissipate its effects." In no other field of preventive practice is there more hope of success than in the science of nutrition.

CHAPTER XIII.

CATEGORY III: EXOGENOUS CHEMICAL AGENTS.

THE PROCESSES OF POISONING AND INTOXICATION.

THE dictionary definitions of a poison are too inclusive to permit the use of all substances which they embrace as categorical causes of disease because they include the noxious chemicals which develop within the organism; *i. e.*, the endogenous poisons. Although the split-protein products that arise in the gastro-intestinal tract and the harmful products of metabolism, such as the toxic substances of uremia and diabetic acidosis, are poisons, they do not arise *de novo;* they have an antecedent history in the disease processes in which they are concerned and do not of themselves initiate pathogenesis. As poisons they are incidental factors which may or may not arise in the course of pathogenesis, and this in any given instance is not inevitable and dependent on their presence. It is necessary therefore that a true chemical poison which can initiate disease must originate outside of the organism; *i. e.*, in its external environment. (It is a specious argument to say that the lumen of the gastro-intestinal tract is external. Although substances in the lumen have not yet been assimilated and entered into body cell activity they have been influenced by, and taken part in, many digestive mechanisms.)

Distinction must be made between the chemical substances of the nutritive elements and those of the external poisons. It has been shown that the nutritive elements serve a useful purpose in the growth, development and repair of body tissues by virtue of their chemical nature. Exogenous poisons are also chemical substances, and their action involves chemical change, but they serve no useful purpose and do harm. There are some chemical substances that can be placed in both categories because at times they serve nutrition and at others act as chemical poisons. Iodine is an example of this dual capacity. Iodine taken in physiologic amounts is essential to the normal activity of the thyroid gland but the same element used in another way may cause severe burns. It is not sufficient to say that exogenous chemicals perform no useful function and do harm but to qualify the statement by adding "in the amounts and manner in which they are acquired." Thus, iodine in physiologic amounts and taken by way of the gastro-intestinal tract is a *necessary nutritive element, but when placed on the skin*

or a mucous membrane in strong solution it is an exogenous chemical poison.[1]

The conditions to be satisfied for a substance to be placed in the category of exogenous chemical agents are: it must depend on chemical action for its effects on the body; it must originate in the external environment of the organism; and it must do harm but perform no useful function in the quantity and manner in which it is acquired.

A strict differentiation between chemical and physical action has become impossible. It is customary to consider the intermolecular exchanges of the higher orders as chemical and the subatomic phenomena as physical. Among the chemicals are those which exert their harmful effects on the body by virtue of subatomic energy exchanges. When this is true of a chemical substance, such as radium, it will not be included in the category under discussion but reserved for the section on physical forces and energies.

CLASSIFICATION OF POISONS.

Since the category of exogenous chemical agents requires that the toxic substances approach the organism through its environment it becomes important to know the sources of the poisons and the manner in which they are acquired. Practical application of preventive principles necessitates that barriers be interposed between the poisons and the elements of the organism on which they act. For this reason the most useful classification within this category would be one in which the agents are arranged according to the way in which they are acquired.

The following classification of external poisons and intoxicants aims to present them in a form to which the principles of prevention can be effectively and practically applied:

Exogenous Chemical Agents.—Classified according to mode of acquisition.

I. By Inhalation
II. By Ingestion
III. By the Skin and Other Parenteral Tissues.

THE PROCESSES OF POISONING.

The ultimate effect of all poisons is on the cellular elements of the body. This may be so destructive as to cause the death of cells or so relatively innocuous as to interfere only with their function by

[1] The poisonousness of a substance cannot be considered as an inherent quality of the substance any more than it can be said that man is a murderer. Man may be a murderer under certain circumstances, and any substance may act as a poison under a given set of conditions Even the most useful physiologic substances can produce harm when administered to the body in unaccustomed amounts or manner and when they do so they must be considered as poisons

altering the character of their membranes, cytoplasm, nuclear elements or cytoplasmic extensions.

The extent of damage produced by a poison depends on the nature of its effect on the cells primarily exposed to its action and the relative dependence of these cells on other tissues and functions of the body. Thus the effect of carbolic acid which destroys the cells in a limited area of the body surface remains localized, but when arsenic, chloroform, carbon monoxide, or digitalis are absorbed they not only influence organizations of cells locally but the functions of other systems dependent on them. The processes of poisoning may be as simple therefore as coagulation of the protoplasm of a few almost independent cells or as complex as changes leading to the death of the whole organism.

The normal processes of cells are balanced mechanisms between themselves and the cellular organizations of which they are a part. Poisons act at first as harmful factors in the environment of cells and they may be restricted to this type of activity. Thus a poison *in solution in pericellular fluids may alter the character of the liquid* environment to such an extent that it interferes with the functions of the cell without entering the cell itself. On the other hand the poison may enter the cell from the environment and become a factor in the intracellular mechanisms.

Poisons frequently show selectivity in the cells which they affect so that where they may be poisonous to one cell type or tissue they are not necessarily so to others. This is evidenced by such specificity as the effect of digitalis on the neuromuscular mechanisms of the heart; strychnine on the motor side of the brain and spinal cord; mercury on the kidneys; carbon monoxide on the red blood cells. Selectivity appears to be of the nature of chemical affinity between the poison and the specific protoplasm, but its real mechanism remains unexplained.

Tolerance.—A mildly irritating substance applied to the skin can be dealt with by the tissues in proportion to the ability of the cells to preserve their equilibrium within their limits of tolerance. This may be influenced by individual or local circumstances such as idiosyncrasy or hypersensitiveness to the poison concerned, and factors that favor chemical action, like heat and moisture or the type of skin involved. The conception of cell tolerance is of extreme importance in chronic poisoning. Heavy tobacco smokers, coffee drinkers, arsenic eaters and cocaine habitues probably possess a high tolerance for these substances. So little is known about the intracellular changes which occur on the introduction of a poison that the problem of cell tolerance remains unsolved.

With the exception of the reactions of the body to a small number of the vegetable poisons and snake venoms, and the toxic products of parasites, there is considerable question whether the cells and

tissues produce anti-poisons such as are found in the processes of immunity. It seems best at this time to restrict the use of the word immunity to those processes in which specific antibodies are produced. In some of the occupational dermatoses the apparent sensitivity of the worker to the poison is variable from time to time and some individuals working under the same conditions never show any harmful reaction to it. This is loosely spoken of as immunity, but until it is definitely established that immune bodies are formed against the simple chemical poisons, the apparent immunity to them must be laid to their defense mechanisms.

Landsteiner[1] has recently presented evidence that the reactions to simple chemicals, tissue immunity, and hypersensitiveness may be phases of immune mechanisms.

In the instance of tolerance to arsenic it is shown that the resistance is one of increasing inability of the cells of the intestinal mucosa to absorb the metal, for if arsenic is injected into the body of an "arsenic eater," he is no less tolerant to it than one unaccustomed to its use.

It is probable that tolerance to most poisons is an enhancement of bio-chemical reactions, *i. e.*, certain cells increase their power to oxidize, reduce, dissociate or detoxify poisons which are brought to them in increasing amounts or in small quantities over a long period of time. In many instances there are definite pathologic changes in the cells upon which the entrance of the poisons into the body depends so that the noxious agents can no longer reach the cells and tissues which they would otherwise affect. Where such pathology does not occur the explanation must be sought in the intracellular chemical mechanisms. In these instances marked changes may be apparent in the functions of the cells but they are readily returned to normal. The action of chloroform on the cells of the central nervous system exemplifies such physiologic, but not pathologic change. Morphine also causes physiologic changes in the nerve cells of the brain but they are reversible and the cells maintain their power of restoration against increasing doses of the drug.

MacNider[2] has recently demonstrated in experimental animals that the resistance of fixed tissue cells to toxic substances may be due to a metaplasia. He showed that uranium nitrate given subcutaneously to dogs in varying amounts produced different pathologic changes in the epithelial cells of the convoluted tubules. Dosages of 2 mg. per kilogram body weight produced degenerative changes followed by repair and restoration of normal function. A second injection of the same amount is followed by a repetition of the first changes, the cells evidencing no resistance to uranium.

[1] Landsteiner, K: New England Jour. Med., 215, 1199, 1936.
[2] MacNider, W. deB.. Science, 81, 601, June 21, 1935.

Dogs which received 4 or 6 mg. per kilogram and survived showed metaplasia of the epithelium of the convoluted tubules. Reintoxication of the animals with doses not exceeding 8 mg. per kilogram failed to produce degeneration of the cells. Similar observations were made on the effects of uranium nitrate on liver cells with the same general results. MacNider concludes that "A tissue resistance to certain chemical substances may depend upon the development in tissues, as a process of repair following injury, of an altered type of resistant fixed tissue cell which maintains a sufficient degree of functional effectiveness to enable the organism as a whole to survive."

The elimination of poisons is one of the most important protective mechanisms. This may occur through any one or more of the external excretory or secretory processes.

The deposition and elimination of a poison depends on many factors. In some cases mechanisms for ejection come immediately into play, such as vomiting, diarrhea and coughing. Diluents may be poured out from secreting surfaces and be sufficient to mitigate the effect of the poison completely. When a poison has an affinity for some special type of cell or tissue there is a tendency for it to concentrate at that point and its subsequent disposition and elimination will depend on the metabolic processes and relations to excretory mechanisms of the tissues concerned. Thus, lead tends to accumulate in osseous tissues and is eliminated in the activities of bone and mineral salt metabolism. Arsenic is stored, reabsorbed and restored several times over in the liver, and will be lost to the body only as it becomes involved in some secretory or excretory process. The fate of poisons is greatly dependent on their physical state. Volatile substances have a fleeting action and are lost very rapidly through the respiratory circuit, whereas colloidal and particulate substances are more often taken up by phagocytic cells and their stay in the body is thus prolonged. The physiologic activity of tissues and organs at the time that the poison reaches them has a bearing on their effect; thus it is known that there is less danger of absorbing lead from the stomach in the presence of active digestion of food. Pre-existing pathology can alter the elimination of a poison by changing the course through which it would ordinarily pass into other channels. The recalcitrance of the mucosal cells of the intestine to arsenic may be an example of this shunting effect. The dissociation products of poisons are so varied as to preclude any generalizations on their final channels of elimination.

From the foregoing discussion it can be seen that exogenous chemical agents have a diversified and sometimes highly complicated natural history. The story of lead poisoning is an example of how much of its natural history is concerned with the sources from which it is acquired. From the preventive point of view this

becomes of more importance than the full knowledge of its harmful effects within the body.

Nevertheless, complete understanding of a poison must include its entire natural history. At present, knowledge of most poisons is limited to fragments of their natural histories but enough is known of their sources, the ways in which they ate acquired, and their modes of action to permit effective prophylactic measures against them.

POISONS ACQUIRED BY INHALATION.

The process of breathing-in is the only essential requirement in this classification. It is not necessary that the harmful substances affect the respiratory system in any way. The agent may be entirely innocuous to the structures of the nose, throat or lungs, and need not even enter the body through the linings of these parts. Thus, lead dust in the air may be inhaled and accumulated in the nose and naso-pharynx but it does not follow that lead poisoning results from absorption at these points. On the contrary the lead dust is washed into the pharynx by the secretions of the nose, mouth and throat and is then swallowed.

The corollary to the requirement that the noxious agent be acquired by inhalation is that it must be respirable, that is, in a condition to be inspired. Gases, particulate matter in suspension in the air, and vapors, harmful in themselves or containing toxic substances in solution in their droplets, are the forms in which poisons can be inhaled. The mechanisms of poisoning by inhaled agents are determined by the specific chemical reactions between the poison and the cells concerned, and for this reason, differences are found between the effects of the same substance entering through different portals and thus first meeting with different cells and tissues. It is of greatest importance therefore to know that a given poison may be acquired through inhalation. Furthermore, the protective mechanisms against the entrance of a poison through the respiratory tract differ widely from those of other channels of entry.

Preventive measures against inhaled poisons must take cognizance of the manner in which they get into the respirable state. While it will be impossible to enter fully into the discussion of all of the factors involved in each poison, emphasis will be placed on where and how it exists in the environment and through what processes it becomes inhalable.

Noxious Gases, Vapors and Fumes.—Carbon Monoxide (CO).— The oldest source of carbon monoxide historically, is from the incomplete combustion of smoldering or banked fires.

With the advent of the use of peat and coal for fuel the probabili-

ties of carbon monoxide poisoning increased so that stokers and fire tenders became frequent victims. The domestic coal stove and furnace have furnished many fatalities.

Illuminating gas from either natural or artificial sources has been the most common cause of carbon monoxide deaths. In the United States it accounted for 917 deaths in 1932. Some of these were suicide.

Accidental deaths from illuminating gas in homes result from leaking pipes, faulty meters, and the flow of gas from an unlit jet. In the last instance, the light may be blown out, the gas may be accidentally turned on by jarring a loose key, or the gas pressure may fall so low as to permit the light to be extinguished by a draught of air.

Carbon monoxide is a common menace in deep mines where it is produced in large quantities from blasting, explosions and mine fires.

The internal combustion engine gives off large amounts of carbon monoxide through its exhaust. In closed garages without ventilation the gas may accumulate so rapidly as to cause death in a very few minutes. It is estimated that in the average size private garage (10 by 10 by 20 feet), an engine running at idle for the purpose of warming-up on a cold day will give off enough carbon monoxide in three minutes to produce definite toxic symptoms and may cause death in five minutes. This fact has become so generally known that it has been turned to account as a means of suicide.

It is seen then, that carbon monoxide poisoning may occur under most varying and unsuspected circumstances. The only single generalization that can be made about its origin is that it always *results from the combustion of hydrocarbons and that the combustion is incomplete.*

Carbon monoxide is inhaled directly and is absorbed through the alveolar mucous membrane. There is no protective mechanism in the upper respiratory tract which can influence its concentration or chemical character in any way. The only prerequisite to poisoning is the concentration of carbon monoxide in the inspired air and the time over which it is inhaled. It is variously estimated that concentrations of 0.2 to 0.5 per cent is irrespirable, but amounts less than this may still be poisonous. Henderson and Haggard[1] combine the factors of time and concentration to arrive at a toxic index. They state that "when the time of exposure in hours multiplied by the concentration of carbon monoxide in parts per 10,000 of air equals 3 there is no perceptible physiologic effect; when it equals 6 there is just a perceptible effect; when it equals 9, headache

[1] Henderson, Y., and Haggard, H. W.: Rep. (N Y.) State Tunnel Com , 1921. See also, Rosenau, M. J., *Preventive Medicine and Hygiene*, D Appleton & Co., New York, 1931, p. 857.

and nausea are induced; and when it equals 15 or more the conditions are dangerous." It is obvious that any knowledge of concentration can be had only when the conditions under which it is produced are relatively fixed. This can be estimated in some of the industries but can rarely be anticipated in providing for proper ventilation in buildings where coal-fuel and illuminating gas are in use.

The poisonous effect of carbon monoxide is due to its chemical affinity for hemoglobin which is some 300 times greater than that of oxygen. Because of this the oxygen is crowded out as it were in favor of the carbon monoxide and the tissues in general suffer from anoxemia. The carbon monoxide does not affect any of the cells directly, and the respiratory failure, weakness, headache and all other symptoms are due to the deprivation of oxygen. It is said that even the erythrocytes are not harmed. Carbon monoxide is not stable and as soon as the source of carbon monoxide is cut off the combination in the blood is broken up. Generally, therefore a person who does not die immediately from an acute attack from this gas will recover if he is removed to a carbon monoxide-free environment. The sequelæ of carbon monoxide poisoning are the results of tissue damage done at the time of anoxemia and not due to the retention of carbon monoxide.

Carbon monoxide has no cumulative effect and any chronic poisoning due to it can result only from continued low grade exposure. The headache, weakness and nausea occasionally seen in garage workers and furnace and oven tenders is not so much a chronic gas poisoning as a chronic exposure to poisonous gas. It is alleged that policemen stationed at busy traffic centers may suffer from such so-called chronic carbon monoxide poisoning. Measurements of carbon monoxide in the atmosphere of city streets reveal considerable amounts of carbon monoxide and it is not too much to expect that it may have some influence on those exposed to it continuously.

Tobacco smoking has recently come within the possibility of causing mild symptomatic effects from carbon monoxide. There is undoubtedly a considerable amount of carbon monoxide generated in the smoldering cigar, cigarette and pipe and those who inhale mouthful after mouthful of smoke must take in some of this gas. Gettler and Mattice[1] have shown a definitely higher concentration of carbon monoxide in the blood of tobacco smokers than nonsmokers.

It must be re-emphasized that these are very low grade concentrations and the anoxemia must necessarily be of the same order and probably very temporary.

Carbon monoxide is colorless and odorless and is non-irritating to the respiratory passages. The first indications of its presence in

[1] Gettler, A. O., and Mattice, M. R.: Jour. Am. Med. Assn., 101, 92, 1933.

toxic amounts are due to its effects on the blood and tissues. In acute poisoning these are so rapid that a dangerous state may be reached without warning and this, combined with an early inability to call for aid or to help oneself, makes carbon monoxide one of the deadliest of poisons.

Carbon Dioxide (CO_2).—The most common source of carbon dioxide poisoning is in mines where this gas accumulates as the result of the action of air on oxidizable material.

In conjunction with nitrogen (87 per cent), carbon dioxide (13 per cent) it makes up the dread "black damp" of mines. It occurs in any closed space where the products of oxidation can accumulate and is therefore found in wells, vats, silos, caves and other ill-ventilated, confined spaces.

While it remains as a definite danger in these places its concentration in poorly ventilated rooms in amounts sufficient to produce ill-effects is considered much less likely than was formerly supposed. The explanation of the malaise, dizziness, etc., commonly complained of by people in crowded quarters is now generally laid to other environmental factors. Even in mines, many of the harmful effects are to be attributed not so much to the increase in carbon dioxide as to the decrease in oxygen. The concentration of carbon dioxide in air, necessary to produce detrimental effects is about 7 per cent, although lower figures may cause discomfort. It requires over 20 or 30 per cent to be dangerous to man.

Carbon dioxide is a strong cerebrospinal stimulant and under normal conditions is responsible in large part for the processes of respiration. Poisoning from carbon dioxide is an exaggeration of this effect. Like carbon monoxide, the double oxide is non-irritating to the respiratory epithelium and is not a tissue poison.

Under average conditions carbon dioxide rarely accumulates in public rooms, sleeping quarters, etc., in concentrations above one-half of 1 per cent. In certain industries which deal with the oxidation and fermentation of vegetable substances, such as in the manufacture of beer, the concentration may rise to 3 or 5 per cent and very rarely to as much as 12 per cent. At the lower figures workmen have no complaints which could be attributable to carbon dioxide.

Acute carbon dioxide poisoning is therefore largely confined to mining and the less frequent accidents in other industries. Deaths have been reported of men who were working in empty linseed oil vats, and in wells and sewers. It is almost entirely an industrial hazard.

Hydrocyanic Acid Gas (HCN). **Prussic Acid.**—Volatilized hydrocyanic acid may arise from the acid itself or by displacement from its salts. In this form it is colorless, and possesses an odor of peach blossoms or oil of bitter almonds.

The pure acid is seldom seen outside of the laboratory, that which

is sold in pharmacies usually being a 2 per cent solution or as Sheel's acid in the strength of 4 to 5 per cent. Sufficient volatilization may arise from the pure acid to be a danger to laboratory workers but the weakness of the commercial dilute acid possesses little danger of poisoning from its fumes. The salts and salt solutions of hydrocyanic acid are unstable and the cyanid radicles are readily displaced by air so that smelling and breathing these chemicals is always potentially dangerous. Potassium cyanid is used by photographers, lithographers and electrotypers. Although it is employed by them in solutions which are relatively harmless insofar as the amount of poisonous vapor they give off is concerned, there is always some danger in the preparation of the solutions from the pure salts.

The deliberate generation of hydrocyanic acid gas in large amounts is seen in fumigation. It is produced by dropping sodium cyanid into a dilution of commercial sulphuric acid in water. (One ounce of sodium cyanid to each $3\frac{1}{2}$ ounces of a mixture of sulphuric acid, $1\frac{1}{2}$ ounces, in 2 ounces of water.) The amount of sodium cyanid used to produce a sufficient concentration of hydrocyanic acid gas varies with the purposes for which it is intended. The destruction of mosquitoes is accomplished in one-half hour by one-half ounce of sodium cyanid per 1000 cubic feet of space to be fumigated, while lice are killed only after an exposure of two hours to gas produced from 10 ounces of sodium cyanid per 1000 cubic feet. Because of the rapidity with which this gas is generated and its high volatility the workers must either drop the sodium cyanid (bag and all) into the sulphuric acid solution on the run, or resort to some mechanical tipping device which can be operated at a distance. Most fatalities have occurred among workers who have entered the fumigated space before all of the gas had been removed by ventilation. Cyanogen chloride has recently come into use as a fumigant. It is highly toxic and penetrating but less lethal than hydrocyanic acid. An advantage in its use lies in its irritating and lachrymating properties which give warning of its presence in less than fatal amounts.

Many cases of mild and severe poisoning are reported among silver and gold cleaners and platers. In these instances the moist cyanid salts give off sufficient hydrocyanic acid vapor to be inhaled in harmful quantities.

The toxic action of hydrocyanic acid depends upon its direct effect on protoplasm and indirectly upon asphyxia brought about by the formation of cyanhemoglobin, a stable compound which reduces the oxygen carrying capacity of the erythrocytes. The blood is rendered a bright red.

Nine-tenths of a grain of anhydrous hydrocyanic acid has been known to produce death but the minimum lethal dose is generally regarded as nearer 3 to 5 grains. This latter dose is equivalent to 45 minims (3 cc.) of the official dilute acid. The single salts of

prussic acid are less toxic than the acid but their effect is the same. The double salts, such as potassium ferrocyanid, are non-toxic.

Hydrocyanic acid is one of the most rapidly acting poisons known but death is seldom as instantaneous as reported. Most deaths occur within two minutes to one hour. An overwhelming inhalation of hydrocyanic acid gas may appear to produce death almost instantaneously, but there is probably always a short latent period with unconsciousness. The cyanid salts show a much more prolonged fatal period and death may not occur for twenty-four hours.

Detoxification of cyanid in the body is brought about by combination with sulphur to form the sulphocyanids. These compounds are eliminated largely through the kidneys but also appear in the saliva. Chronic cyanid poisoning is accepted as a possibility by many. It is probably a rarity and it is likely that many instances are not due to inhalation of volatile hydrocyanic acid but to ingestion of very small amounts of the salts. A tolerance to cyanid has never been described. Those who cannot accept the possibility of chronic cyanid poisoning base their scepticism on the fact that health examination of employes in factories where solutions of hydrocyanic acid were in constant use showed no discoverable disturbances of health and also because small amounts of the acid are readily converted into harmless sulphocyanids. There can be no question that many workers receive sub-lethal doses on occasions, but this does not imply cumulative or progressive chronic poisoning.

Suphur Dioxide (SO_2).—This is an irritant gas with the odor of burning sulphur and its presence in the air depends upon processes in which sulphur is burned or in which sulphuric acid is produced or employed. Two of the earliest of these processes were the use of sulphur dioxide for fumigation and the manufacture of sulphuric acid. In the former, sulphur candles were burned in sealed rooms with the liberation of sulphur dioxide and in the latter sulphur dioxide was formed by roasting pyrites in the old "lead-chamber" process.

Sulphur dioxide is now used in the bleaching industries and is employed in the chemical types of household refrigerators. Under ordinary circumstances the sulphur dioxide in these processes is produced within sealed chambers and poisoning should occur only through carelessness, accidents or faulty mechanisms.

Due to its irritating properties, the inhalation of sulphur dioxide results in a spasmodic reflex contraction of the glottis. Even in dilutions of 0.01 parts per thousand of air the irritation may be severe enough to produce this reaction. Much less than that amount will act as a warning by throat and eye irritation.

Sulphur dioxide is soluble in the water on the surface of the mucous membranes of the respiratory tract and this solution results in the formation of sulphurous (H_2SO_3) and then sulphuric (H_2SO_4) acids.

The latter acid is highly caustic and most of the subsequent symptoms and pathology, edema, congestion, pneumonia, dyspnea, cyanosis, collapse, are due to this added effect.

There seems to be a tolerance to sulphur dioxide, for many workmen become accustomed to working in atmospheres 3 or 4 times as concentrated as that under which they first began work and which produced uncomfortable irritation. The sulphuric acid is eliminated in the respiratory tract secretions.

Hydrogen Sulphide (H_2S). Sulphuretted Hydrogen.—When organic matter decomposes under natural or artificial conditions a putrid gas with the odor of rotten eggs is given off. This gas is hydrogen sulphide. It is colorless, transparent, little heavier than air, and burns with a blue flame.

There is a surprisingly large number of occupations and situations under which sulphuretted hydrogen has been generated unsuspectingly in concentrations sufficient to cause death. A few of the more common are: sewers and drains, sludge pits, fat rendering plants in the manufacture of soap, illuminating gas works, well cleaners, glue and lubricant manufacturers, the manufacture of coal-tar dyes and barium trisulphide (a parasiticide), mineral-water bottling works, mines (from pyrites), smelting processes, streams and lakes contaminated with sewage, and in some ground water gases.

Many cases of poisoning have resulted from the fact that there is such a small difference between the amount detectable by its odor in the air and the concentration which produces toxic symptoms. Although amounts as small as 0.1 parts per 1000 can be recognized by its characteristic smell, 0.5 parts per 1000 may be rapidly fatal. Concentrations higher than 2 or 3 parts per 1000 cause almost instantaneous death. Inhaled hydrogen sulphide is absorbed immediately into the blood stream where according to Haggard[1] it is transported in a loosely combined state and produces its toxic effects by direct action on nerve tissues. Its first action appears to be a stimulating one on the afferent vagus fibers. This produces hyperpnea of a severe grade which results in excessive carbon dioxide loss and eventual death through complete apnea. Small doses of hydrogen sulphide which are only mildly toxic can apparently be oxidized and reduced through the formation of sodium sulphide.

Hydrogen sulphide is only slightly less rapidly fatal than hydrocyanic acid, the higher concentrations causing almost immediate death. Lesser amounts may cause unconsciousness from which the patient recovers without any apparent residual effects. Still smaller doses produce marked irritation of the exposed membranes of the

[1] Haggard, H. W., and Charlton, T. J., Jour Biol. Chem., 49, 519, 1921.

eye and entire respiratory tract and slight toxic symptoms such as nervous irritability, headache, dizziness, fibrillation and cold sweats.

Bronchopneumonia is a not infrequent sequela of non-lethal poisoning.

Chronic sulphide poisoning manifests itself in very much the same way as the single small dose and it is likely that the alleged chronic forms are only repetitions of such small doses. There is no evidence of any cumulative action from this gas but reports indicate an increasing individual susceptibility to it after repeated exposure.

Carbon Disulphide (CS_2).—The vapor of liquid carbon disulphide is given off at ordinary room temperature and possesses a sweetish odor not dissimilar to chloroform. It is inflammable and heavier than air.

Inhalation of this toxic gas occurs most frequently in the rubber industry where immense quantities are used as a solvent vehicle for sulphur monochloride in the cold vulcanizing process. It is used also as a solvent for oils and fats, as a disinfectant, and in the manufacture of artificial silk.

Toxic effects may be produced when the concentration in the air is 1 part per 1,000,000. Twice this amount produces immediate and prolonged intoxication and 3.5 parts per 1,000,000 cause severe symptoms and early unconsciousness. Fatal acute cases are practically never seen and the main problem today has resolved itself into the cases of chronic prolonged intoxication.

Carbon disulphide produces a methemoglobinemia with destruction of the red cells. Its symptomatology is due to overstimulation and then depression of many parts of the nervous system. Continued exposures, leading to chronic poisoning, reveal themselves in increasing nervous excitability which may reach the proportions of insanity.

Recovery from chronic carbon disulphide poisoning is slow and may require a year or more away from the occupation in which it was acquired. Paralysis may be permanent.

The insidious nature of small exposures makes it necessary for physicians in private or industrial practice to keep the possibilities of chronic intoxication in mind in all cases showing nervous and mental derangements due to unexplained or insufficient causes. Inquiry by the private practitioner in industrial regions into the nature of materials with which his industrial patients come in contact should aid materially in diagnosing obscure neurologic conditions.

Benzol (C_6H_6). **Benzene.**—Benzol or benzene (*not* benzine, a petroleum product) is formed from the distillation of coal-tar and finds its greatest use as a solvent for gums, fats and resins. It is highly

volatile and its vapor is 3 times as heavy as air. It possesses a pleasant, non-irritating odor.

Because of its solvent qualities and its high, rapid volatility it finds wide usage in the manufacture of products where gums and resins are to be dissolved and quick drying is desired. Latex (crude gum rubber) and lac, dissolve readily in benzol and it is therefore used in the rubber, varnish and lacquer industries. Its quick-drying properties make it an ideal solvent for paint and varnish removers. It is also used in the manufacture of fabrikoid, artificial leather, linoleum, shoe cement, as a coating for leather upholstering and automobile tops, in the preparation of synthetic carbolic and picric acids and in anilin dye works. It is also used in the manufacture of cement for sanitary food cans and in the photographic film industry.

Controversy still exists as to whether the pure or crude benzene is the most toxic. Most investigators feel that crude benzene is the most poisonous of the two and that it is probably due to the presence of its two homologues, toluene and xylene.

The danger of benzol poisoning is due largely to the necessity of its open use in some stage of most processes in which it is employed. Being highly volatile, an amount sufficient to be toxic can escape from an open container in a very short time. It is obvious that the use of the liquid as a paint remover or dry-cleaning fluid affords ready opportunity for inhalation of the fumes.

The dangerous concentration in air begins at about 1 part per 100,000. Exposure to 2 or 3 parts per 100,000 for a few hours is decidedly toxic and may cause unconsciousness.

Benzol may cause acute or chronic poisoning. In the acute form the toxic effect is one of damage to the respiratory epithelium and the nervous system. Chronic poisoning depends to a great extent on individual susceptibility but aside from this there is apparently some unknown factor which makes poisoning more likely under certain circumstances than others.

Benzol is a strong leucotoxin, destroying the white cells in the circulating blood and the blood-forming organs. It also affects the erythroblastic tissues and produces an aplastic anemia. Some destruction of the adult erythrocytes also takes place.

Benzol is eliminated from the body by its oxidation to phenol, catechol and quinol. It is excreted as phenol sulphates by the kidneys and unchanged through the lungs.

Nitrobenzol (Nitrobenzene). Essence of Mirbane.—The liquid form of nitrobenzol is employed in the chemical industries in the manufacture of synthetic perfumes, anilin, explosives, soaps, flavoring extracts and drugs. Poisoning from the fumes is rare compared to that produced by contact or ingestion. For this reason the

toxicologic details are discussed in more detail in the section, Poisons Acquired by Contact.

Chlorine (Cl).—Chlorine gas is two and a half times as heavy as air and in concentrated form possesses a yellowish-green color. It is readily recognized by its pungent, acrid odor.

The gas is used in industry either in the pure form in steel cylinders, or in combination with salts as the common bleaching powders. Some plants manufacture their own chlorine by electrolysis. Chlorine is given off in the early processes in the manufacture of nitric acid.

Before the mass poisonings from chlorine as a war gas, cases of chronic and acute exposure to this irritant gas were seen most commonly in those industries where bleaching was carried out on a large scale. This gas is still used in making the finer grades of paper, calico-printing and some dye industries, and in plants manufacturing disinfectants, bulk chlorine and bleaching agents.

Poisoning occurs from exposure to small amounts of the gas arising from chemicals in which the chlorine is loosely combined, leaks in the apparatus in which chlorine is generated or in use as the pure gas, accidental exposure to overwhelming quantities of chlorine through breaks in generators or containers, or by workmen entering chambers before the gas has been expelled.

Inhaled chlorine acts primarily as an irritant to the respiratory mucous membranes. In small doses it produces an unpleasant, choking sensation without any general symptoms. In higher concentrations a definite sense of suffocation is produced with cough, spasm of the glottis and difficulty in breathing. Massive exposures result in such intense inflammatory response of the bronchial mucosa that the exudate fills up the lungs and causes death by asphyxiation.

The established limit of concentration of chlorine in the air which is considered dangerous is 1 part in 100,000. One part in 10,000 may cause death if inhaled over a period of one or two hours. One part in 1000 may cause death in as short a time as five minutes.

Phosgene (COCl). **Carbonyl Chloride.**—Although phosgene is better known as a "war gas," poisonings have occurred in industry.

Phosgene was formerly prepared by exposing a mixture of carbon monoxide and chlorine to sunlight. It is a colorless gas which reveals itself, if at all, by its musty odor. In pure form it lacks any subjective irritating qualities in the upper respiratory tract. In the smaller bronchioles it is hydrolyzed in the moisture of the lungs with the formation of hydrochloric acid. Aside from its preparation as a war gas, phosgene occurs in the process of manufacturing certain dyes, especially as an intermediate product in the process of making Michler's ketone.

Phosgene is one of the products remaining after the use of carbon

tetrachloride fire-extinguishers and several fatalities have resulted following mine and ship fires in which this chemical was used.

The toxicologic effects of phosgene are due to the hydrochloric acid produced in the smaller radicles of the bronchial tree. An acute inflammatory exudate is poured out, which if sufficient enough, may produce death from asphyxia. The congestion and edema of the mucous membranes may not come about for several hours after exposure.

Mustard Gas $(C_2H_4Cl)_2S$. **Dichlorethyl-sulphide, Yperite.**—This gas is not an industrial or domestic hazard except as poisonings may occur in its manufacture for war purposes. It is a heavy colorless gas which does not betray its early presence by local irritating effects. Some of its more disabling properties are due to its effects on the skin. (See Poisons Acquired by Contact.) When inhaled, mustard gas produces an acute edema and a delayed bronchopneumonia. Absorbed mustard gas produces general symptoms which are suspected of being due to the liberation of hydrochloric acid which affects the body cells.

It is stated that a concentration of 1 to 13,000 parts of air, breathed for five minutes, will prove fatal.

Petroleum Distillates.—Naphtha, Benzin, Petroleum Ether.—These are only a few of the many products obtained in the fractional distillation of petroleum. They all give off volatile vapors which can bring about acute or chronic poisoning. All are inflammable.

Poisonings from these vapors are encountered around oil wells and distilleries, storage tanks and distillery vats, and in industrial processes in which these substances are used. Naphtha is used as a solvent for rubber, in the bronzing industry, as a degreaser of fertilizer and leather, and in the manufacture of furniture polish, gilt, metal polish, paint, shoe finishing, and waterproofing. Benzin is a constituent of quick-drying paint, dry-cleaning fluids, and automobile gasoline fuel. Because of its high solvent action on fats and resins it is employed in very much the same industries as the coal-tar derivative, benzene.

Naphtha acts as an acute intoxicant to the central nervous system, the early stages being ushered in by what is known as a "naphtha jag." The patient becomes hysterical and silly with uncontrollable laughing or symptoms of expansion. A maniacal state has been described in some instances. Irritability of temper from slow dosage during the day, is reported by one foreman. Nervousness and trembling and an inability to perform fine hand-skill work is common. Severe poisoning results in collapse with loss of consciousness, cyanosis and drop in temperature.

There is some question whether there is a true chronic naphtha poisoning but considerable evidence points to it as a fact. Workers around rubber industries are reported to have a higher sickness rate

than control groups and show a general loss of health with indigestion, restlessness and irritability, headache, attacks of dizziness and constipation.

Benzin and petroleum ether poisoning have been seen among men cleaning out tank cars and vats, and those working around gasoline motors in confined spaces. Headache and dizziness are common complaints among garage and automobile repair men and they are attributed to the gasoline fumes. Painters using quick-drying paints are subject to the same effects, especially when working in closed rooms or where the temperature of the paint has been raised to aid in drying.

Turpentine.—Oil of turpentine is a distillate from oleoresins of pine wood and contains several of the terpene hydrocarbons ($C_{10}H_{16}$). It is highly volatile and the vapors are toxic.

In the occupations, turpentine poisoning is seen most frequently among those handling paints and varnishes to which the oil of turpentine has been added as a thinner. The petroleum industry has furnished cheaper thinners such as naphtha and petroleum ether, and their increased use in place of turpentine has resulted in fewer poisonings from the latter.

Poisoning from turpentine is far more likely where the painting is done in poorly ventilated places, such as the holds of ships, small interiors, the inside of storage rooms, vats, and similar places without openings.

Acute poisoning produces an intoxication which peculiarly becomes worse on reaching the open. Dizziness is sometimes so overwhelming that painters fall from their scaffold before they can be warned. Spray-guns used in the open may readily permit the inhalation of large amounts of turpentine.

Prolonged exposure in the painting trade may produce a marked secondary anemia, constipation, anorexia and albuminuria. The latter finding is common in acute and chronic cases and is evidence of renal damage. There is not sufficient information at present to be able to say that turpentine acquired in this way will produce a permanent or progressive type of nephritis.

Ammonia (NH_4).—Ammonia vapor is a powerful irritant gas with a pungent penetrating odor. It is lighter than air. The volatile gas may be given off under certain conditions from concentrated solutions of ammonium hydroxide or from its combinations in salt form (ammonium carbonate especially).

Ammonia gas is encountered in greatest bulk in refrigeration plants, and serious and fatal accidents have occurred from breaking pipes and slow leaks in closed spaces. It is becoming more commonly used in household refrigerators, thereby adding another hazard to the home.

Household ammonia is either a solution or a salt. Occasionally

there is sufficient gas liberated from these forms to produce unpleasant irritation of the nose and throat.

Large inhalations of ammonia produce dryness of the throat, larynx and trachea. The inflammation may be so pronounced as to produce edema and suffocation.

Ronzani[1] and Lehman have found an interesting reduction in resistance to anthrax, tubercle bacillus and diplococcus of Frankel infections in dogs which had been subjected to doses of ammonia fumes below the danger limit over a prolonged period of time.

Arseniuretted Hydrogen (AsH_3). Hydrogen Arsenide, Arsine.—Arsine is a colorless gas, and its presence in the air is recognizable only by its garlicky odor and then only when it is in dangerous concentrations. Industrial poisoning from arseniuretted hydrogen is met with under those conditions in which sulphuric or hydrochloric acid come in contact with the heavy metals when either the acids or metals contain arsenic as an impurity. Hamilton[2] says "such conditions are very common in industry, but the fact that people are not looking for this poison explains why so few cases have been reported in the literature, especially in that of this country. It is probable that when an accident does occur the acid fumes are held responsible."

Hamilton reports cases occurring under the following circumstances: Manufacture and extraction of chemically pure acids; cleaning of iron tanks which had held acids, manufacture of hydrogen and zinc dust and hydrochloric acid, balloon making, laboratory workers, the manufacture of vanadium steel, production of zinc chloride and bleaching powders, dipping iron sheets for galvanizing and zinc plates for bronzing, electric storage plants using lead grids immersed in acid, the cyanide process for recovering gold and silver, shipping ferrosilicon in the cargo of ships, and from the lead plates in the batteries of submarines.

Dubitsky[3] believes that danger of poisoning begins when the air dilution is 1 part in 2000.

As stated above the characteristic odor is frequently lacking when poisoning occurs and the case may have progressed to a serious extent before the nature of its cause has been found out; or the cause may never be discovered. A delay of hours or even days may occur between exposure and onset of symptoms, making it still more difficult to connect cause and effect.

Arsine acts primarily by destroying red blood cells. As a result the oxygen-carrying capacity of the blood is acutely reduced and the common symptoms of general anoxemia occur—weakness, dizziness, headache.

[1] Ronzani, E.: Arch. f. Hyg., 70, 217, 1909.
[2] Hamilton, Alice: Industrial Poisons in the United States, New York, Macmillan Company, 1929.
[3] Dubitsky: Zentralbl. f. Gewerbhyg., 8, 121, 1920.

Formaldehyde (H.C.H.O.).—This is a colorless gas of a density almost equal to that of air and possessing an acrid, irritating odor. In solution in water (40 per cent) it is known as Formalin.

Contact with the raw gas is met with most commonly in disinfection processes and in certain industries where it is produced in large amounts. Formaldehyde is employed as a disinfectant by releasing it in closed chambers containing the materials to be sterilized. It is a powerful germicide but a weak insecticide. Industrially, formalin is combined with ammonia in the manufacture of hexa-methylenetetramine (Urotropine), and with phenol to make Bakelite, a hard-rubber substitute.

Poisoning from formaldehyde gas is almost entirely limited to an irritant bronchitis or bronchopneumonia.

Brunnthaler[1] believes that it is a cumulative poison and that poisoning results in increased susceptibility to subsequent exposures. The gas taken into the body goes into solution as formalin, is stored as a methyl compound and is oxidized to formic acid in which form it is eliminated. Various lesions of the liver and kidney and an ulcerative arteritis are alleged to be due to the action of these intermediate products.

Acrolein. Acrylic Aldehyde.—Acrylic aldehyde is an irritating heavy fume liberated in the rendering of fats and oils. It is met with in the soap and varnish industries and in the reclamation by melting of printers' type plates which are covered with oily ink.

The fumes are so obviously irritating and obnoxious to workmen that they cannot remain exposed to them for any length of time. Its physiologic action is that of a powerful respiratory irritant which may produce a bronchitis or bronchopneumonia with profound edema.

Sulphuric Acid Fumes (H_2SO_4).—Sulphuric acid poisoning may be produced indirectly under those conditions in which sulphur dioxide (SO_2) or sulphur trioxide (SO_3) are inhaled, by the conversion of these gases into the acid when they come in contact with the moisture of the respiratory tract (See Sulphur Dioxide).

Poisoning from preformed sulphuric acid occurs in a few industries where the acid is volatilized in various processes. In the celluloid industry sulphuric acid is used as a dehydrant and the fumes of the acid itself may be produced in toxic amounts.

Hamilton lists the following processes in which dilute sulphuric acid is used: (1) manufacture of phosphate fertilizer, (2) petroleum refining, (3) making nitro-cellulose, celluloid and nitroglycerine, (4) pickling iron and steel, (5) general chemical and metallurgical processes.

In all of these the free sulphuric acid fumes or the sulphur dioxide or trioxide which becomes converted into sulphuric acid in the body

[1] Brunnthaler, J.: Zentralbl f Gewerbhyg., 2, 24, 1914.

act as mucous membrane irritants, and if sufficiently concentrated, as corrosives.

Workmen develop a tolerance to low concentrations of the gas. Whereas 1 part in 100,000 in air may be highly irritating to new workers, the older men at the trade may feel no injurious irritations at 3 or 4 times this amount.

Hydrochloric Acid Fumes (HCl).—Volatilized hydrochloric acid or the acid held in fine suspension in droplets of moisture is a powerful upper respiratory irritant. The immediate spasm of the upper air passage which it produces prevents its entrance in any large amounts into the lungs. The irritation is so great as to amount to actual pain. It is fortunate that its distinctive odor in low concentrations acts as a warning to those exposed to it.

Hydrochloric acid fumes are liberated in the manufacture of certain anilin dyes and indulin and in pickling metal. In the latter instance the acid is carried into the air in the droplets from a water spray used to wash steel wire that has been passed through an acid bath. Toxic amounts may be given off in the manufacture of the acid itself from sodium chloride and sulphuric acid.

Nitric Acid and Nitrous Fumes.—Nitric acid and the fumes of its oxides (nitrous and nitric oxide) are powerful physiologic irritants to the respiratory tissues but produce relatively slight symptoms of irritation in proportion to the pathology brought about. A worker may inhale quantities of these fumes and feel little inconvenience other than a mild choking and cough whereas the damage to the lung structures may be severe enough to produce death days later. Investigators have noted a marked difference in the attack rate among workers engaged in the same process at the same time. The tendency has been to ascribe this to differences of susceptibility or tolerance but the mechanisms of the action of the nitrous fumes is too little understood to attempt any interpretation on this basis.

The local effect in the lung is primarily exudative, followed in time by necrosis and/or proliferation of fibrous elements. The latter results in an obliterative bronchiolitis.

The most important observation from the point of view of care of victims is the delay of serious symptoms and even death, hours or days following an apparently mild dose of the fumes.

Nitrous fume poisoning is liable to be encountered in all industries using high nitrogen compounds. Under the present conditions of manufacture poisonings should be due almost entirely to accidents to apparatus. Broken carboys of nitric acid, leaking pipes, faulty gas chambers and carelessness in making repairs to apparatus have been the chief causes of poisoning in the past. Some of these will undoubtedly occur from time to time under the best operating conditions.

The present most common source of poisoning is found in the

nitrocellulose trade. A large number of modern materials in general use are made by the action of nitric acid on cellulose. They vary from moving picture films to varnishes and airplane "dope" and although not harmful in the completed form the workmen employed in their manufacture may be subject to the effects of nitrous fumes.

The International Labor Bureau reports that solutions of nitric acid of more than 15 per cent strength may give off fumes. This acid is used in photo-engraving.

Mass poisonings have been reported in mines following the incomplete detonation of explosives and subsequent burning of the nitrates.

By far the greater number of nitric fume poisonings in the past have been in the manufacture of explosives. War needs created a tremendous demand for nitric acid and explosives and the plants constructed were hurriedly erected and poorly equipped. Precautionary measures were insufficient both because of the pressure of time and the lack of technologic skill available. Peace-time manufacture of gun cotton, nitroglycerin, T.N.T. (trinitrotoluene) and other explosives and the widely used nitro-cellulose has produced a relatively much smaller amount of poisoning due to a better understanding of the dangers attendant on their manufacture.

Anilin Fumes ($C_6H_5NH_2$).—Anilin is an amido derivative of the benzene ring and is a colorless, oily liquid which readily gives off *highly toxic fumes. Volatilized anilin possesses a characteristic* odor and is described as producing a warm, sweet taste in the mouth. Opportunities for volatilization of the oil are many when it is used in open containers in large quantities or when it is subjected to warm temperatures. Sprays of oil readily disperse in fine droplets in the air. Although most of the cases of anilin poisoning are produced *by its entrance into the body through the respiratory tract the* number of cases of poisoning from introduction by other channels are not inconsiderable.

It produces methemoglobinemia and a progressive loss of red cells and hemoglobin. A reduction of hemoglobin to 10 or 15 per cent with stippling of the erythrocytes is said to be almost pathog*nomonic of anilin poisoning.*

Chronic cases which have recovered have been found to have difficulty in returning to their former occupation due to an alleged susceptibility which cannot be overcome.

Anilin poisoning by inhalation of the vapor is found most commonly in the manufacture of anilin itself and of the anilin dyes. Less *frequently workers in the rubber industry where anilin is used as an* accelerator may be exposed to its fumes and poisoning by inhalation is still less common in the manufacture of pharmaceutical preparations, photographic materials and the dyeing industry.

The rôle of anilin in the production of so-called anilin tumors of

the bladder is still under question. Gehrmann[1] is unable to detect any carcinogenic agent in the urine of anilin dye workers. He feels that the agent or agents responsible for the development of these tumors are therefore not in the urine and hypothetically considers the possibility that they are in the systemic circulation and exert their effect at the base of the bladder where the blood supply is richer.

Tetrachlorethane ($C_2H_2Cl_4$) Acetylene Tetrachloride.—Tetrachlorethane is a widely used powerful solvent for cellulose acetate. It is readily vaporized under the conditions in which it is used in industry and possesses a toxicity according to Lehmann[2] 4 times that of chloroform and 9 times that of carbon tetrachloride.

The primary effect seems to be on the bile capillaries and the production of a fatty degeneration of the liver equalled only by that produced by phosphorus. Other German investigators likened its effects to a delayed chloroform poisoning.

Owing to its high solubility for cellulose acetate tetrachlorethane has come into general use in industries employing the former substance. Because it is non-inflammable it is used in the manufacture of moving picture films, varnishes and lacquers. Tetrachlorethane is the common solvent for cellulose acetate in the manufacture of artificial silk, and in France, of artificial pearls. It is also employed in the rubber industry and in the extraction of certain alkaloids and oils.

Hamilton[3] states that workers vary in their susceptibility, but if one is affected even slightly he seems likely to have a severe attack if he is again exposed to the vapors."

Methyl Alcohol (CH_3OH).—Wood Alcohol, Methanol, Columbian or Colonial Spirits.—Methanol, as wood alcohol is now being called by preference, is an alcohol derived from the destructive distillation of wood. It is marketed in pure and impure forms. In the latter it contains more or less of other distillates such as acetone, allyl alcohol, dimethyl acetate, furfurol, or methyl-ethyl ketone. Although some attribute the effects of wood alcohol poisoning largely to these impurities there is now no doubt that pure methanol is a powerful poison acting principally on the higher nerve mechanism of the special senses, especially sight.

Methyl alcohol volatilizes readily at ordinary temperatures and is therefore prone to collect in the atmosphere of poorly ventilated spaces in which it may be used. It is an efficient solvent for varnishes and shellacs, many manufacturers preferring it over ethyl alcohol because of its higher volatility and therefore quicker drying

[1] Gehrmann, G H. *et al.*: Jour. Urol, 31, 126, 1934.
[2] Lehmann, K B. Arch. f. Hyg., 74, 1, 1911.
[3] Hamilton, Alice Industrial Poisons in the United States, New York, Macmillan Company, p. 448, 1929.

time. United States Government Regulations permit ethyl alcohol to be denatured by the addition of methanol but make the restrictions more severe the more nearly the denatured product approaches pure ethyl alcohol. This, unfortunately puts a premium on the use of ethyl alcohol with the higher content of methanol and maintains the hazard to workers with this material.

With the advent of cellulose nitrate in industry the use of methanol as its solvent has spread into many trades. It is also useful as a solvent for gums and resins and methanol either as pure or impure wood alcohol or as a denaturant to ethyl alcohol is used widely throughout the arts and crafts.

Estimates of the toxicity of inspired methyl alcohol run as low as 2 parts per 1000 of inspired air if continued over some time. This is a concentration not difficult to attain when it is used in confined ill-ventilated spaces. A large number of poisonings from this vapor have occurred among workmen who were shellacing or varnishing the interiors of large vats, casks or small storage rooms without provisions for circulation of fresh air. A number of cases of poisoning are on record in which exposure took place under what would ordinarily be considered good ventilation conditions but the concentration of the vapors at the source was so high that workers inhaled them before the gases were carried off.

The manufacture of methyl alcohol itself is not without danger for the "tubs" and condensation chambers must be cleaned out periodically on account of the accumulations of tar and other distillates. The process also carries with it the common hazard of leaking and faulty apparatus.

Although the typical physiologic effect of methanol is on the nervous system and especially the optic tract, workers exposed to the vapor suffer from headache, giddiness, nausea and general ill-health. The reader is referred to the section on Poisoning by Ingestion; Drugs, Medicines, etc., p. 250, for a fuller description of the effect of methyl alcohol on vision. At this point it is only necessary to state that acute or chronic poisoning from the inhalation of methyl alcohol vapor may produce changes of vision ranging from temporary dimness of vision to permanent blindness.

Analysis of mass poisonings reveals a high individuality in susceptibility to methyl alcohol vapors. It is not at all understood why several persons exposed at the same time to apparently the same amount of vapor should not all be poisoned alike but records indicate this to be a fact. It would seem to be important to the industrial physician to keep this in mind for there is further evidence that an individual may be remarkably tolerant to the poison at one time and most unexpectedly be affected by it at another.

Elimination of methyl alcohol from the body is through a slow process of oxidation involving the formation of formic acid. Lactic

and other organic acids are excreted in large amounts during this time and there is a general disturbance of metabolism in the direction of acidosis. Complete elimination may not occur for several days in sharp contrast to the rapid oxidation of ethyl alcohol. Some of the methyl alcohol is believed to be excreted into the stomach and intestines from where it is reabsorbed. There is possibly a cumulative effect which may explain the sudden deaths which have occurred when recovery seemed assured.

Methyl Bromide and Methyl Chloride.—Methyl bromide readily volatilizes and is inhaled without the production of any local irritation or warning symptoms.

Poisonings are reported largely from Continental sources where workmen have acquired it in the preparation for the manufacture of anilin compounds and refrigerants, or in the use or repair of refrigerators.

The symptoms are those of a narcotic poison and may come on very gradually after exposure or with explosive suddenness, with dulness, drowsiness, coma, respiratory distress and convulsions. The pupils are widely dilated. In non-fatal cases there is a prolonged period of incoördination of movement, tremors, unsteady gait, and at times diplopia.

Methyl chloride (chlormethyl or monochlormethane, CH_3Cl) is likewise a narcotic poison and respiratory irritant. It is less toxic than methyl bromide but in heavy dosage brings about a quite similar intoxication.

These two methyl compounds have been shown at autopsy to produce a destructive degeneration of the epithelium of the bronchi which is proved to lead to a purulent bronchitis and pulmonary edema.

Iodine.—Fumes of iodine are given off in large amounts when the crystals are heated to 220° F. At ordinary temperature the volatilization proceeds very slowly being barely perceptible unless the vapor is confined. Concentrated iodine gas is bluish-violet in color and possesses a typical acrid odor. This may be made familiar by inhaling the mild fumes rising from a bottle of iodine crystals.

Iodine vapor is a local irritant to the mucosa of the nose and throat and in large quantities may produce laryngeal or pulmonary edema.

At present, iodine is vaporized in amounts large enough to produce poisoning only in the chemical manufacturing trade and in chemical laboratories. The mild fumes given off during the processing of iodine salts are in too low concentrations to be harmful. Moreover, the fumes are evident and irritating enough to force workmen to call attention to their presence.

Bromine.—The inhalation of bromine vapors in harmful quantities is met with in the manufacturing of tear gas, ethylene, tetraethyl lead and bromine disinfectants. Smaller amounts are encoun-

tered from the gas given off from chemicals used in gold extraction, and the manufacture of films, ink, colors, and dyes.

Bromine gas is heavy and acrid and is highly irritating to the respiratory and conjunctival mucosa.

Mercury (Hg).—In the industries, mercury poisoning is due almost solely to inhalation of its vapors for even pure metallic mercury is constantly vaporizing at ordinary room temperatures. Renk[1] has determined that the air above a pool of mercury one half meter square contained 1.5 mg. of mercury per cubic meter.

Mercury, mercury ores and salts are used in a large number of trades in which opportunities exist for the vaporization of this metal and consequently its inhalation.

The metal occurs in nature as natural quicksilver and as the common ore, cinnabar (HgS—Mercury sulphide). It is in the mining of these two substances that the earliest observed cases of poisoning from mercury vapors are recorded. Present-day methods have not yet completely overcome the high industrial hazards of mercury mining and in recent years rich ore-bearing mines in California have closed down because of the inability to obtain laborers under the conditions in which they had to work.

Heated mercury sublimates, that is it passes directly from the metallic to the gaseous state and back again by immediate condensation. It is not detectable in the air by its smell or local irritating qualities and is therefore insidious in its attack. The absorption of mercury is believed to take place after it has been deposited on the mucous membrane lining of the mouth, naso-pharynx and bronchi and not through the alveolar epithelium.

After absorption the mercury ion unites with the proteins for which it has a high affinity and produces an albuminate which is dissociated with difficulty. As a result the mercury tends to be stored in the body, especially in the bones and liver, and to show a cumulative action. Elimination is therefore slow and takes place by way of the urine and feces. That many glandular tissues partake in its liberation is indicated by mercurial stomatitis, gastro-intestinal disturbances, and the elimination of bile pigment in the urine in cases of poisoning.

Renal and hepatic degeneration are common late results of poisoning, more especially in those cases in which poisoning has resulted from ingestion.

The nervous system is affected almost as seriously if not more so *than the gastro-intestinal tract, especially in the slow, chronic* poisonings. The manifestations may range from irritability and insomnia to major psychoses.

As indicated by the large number of trades listed below in which mercurialism may occur, it behooves the practising physician to be

[1] Renk· Arbeits und Gewerbehygiene, Leipzig, p. 190, 1919

aware of the probabilities of this poison in all cases, men or women, coming under his care for nervous manifestations of any nature.

Mercury poisoning is discussed further under suicidal and homicidal poisons. (See page 240.)

The non-industrial physician is ordinarily quite unaware of the large number of common trades in which mercury is used in such form as to produce chronic poisoning. In the first place it is little known that metallic mercury is constantly giving off vapors under ordinary temperatures. Thus, the wives of workers in mercury-using trades have developed mercurialism through washing their husbands work clothes. It must be kept in mind that the most remote possibilities for poisoning may become imminent probabilities.

All miners of quicksilver or mercury ore are open to poisoning almost without exception and irrespective of the particular process in which they are employed.

The felt hat industry has contributed a large number of poisonings in the past and continues to do so. Mercury compounds of various nature are used in several stages of hat manufacturing, from its use in the stiffening of the hat frames to the coning and brushing processes. At all of these stages mercury in dust and vapor may be inhaled directly or indirectly from impregnated clothing.

The manufacture of thermometers, barometers and other scientific apparatus involves the filling of tubes with metallic mercury. Spill-overs, breakage and leaks result in the accumulation of mercury on tables and benches from which it volatilizes.

Quicksilver backing for mirrors is rapidly becoming obsolete but where used is one of the oldest and most common sources of industrial mercury poisoning.

Mercury poisoning is met with in the manufacture of dry cell batteries through the use of mercury solders; in gold refining and extraction where mercury is employed as an amalgam from which the gold can be readily recovered; in the electrolytic chlorin process and in the manufacture of explosives, fulminants and detonators, incandescent, *x*-ray and mercury-vapor lamps and tubes, paints and artificial flowers, photographic materials, taxidermist's preservatives, and fur fixatives. Dentists who work largely with amalgams are said to be liable to chronic mercurialism whether they handle the amalgam with their fingers or not.

The apparent harmlessness and inert nature of quicksilver itself and the mercurial salts used in industry make it difficult to convince workmen and others of their dangerous nature. This, combined with the slow vaporization at low temperatures and the high volatilization with heat make mercury one of the most dangerously insidious slow poisons. The early manifestations of mercurialism may readily simulate other forms of organic and nervous disease

unless the physician is keenly aware of the possibilities of poisoning from mercury in some of the most common trades and industries.

Lead (Pb).—Lead is inhaled either in the form of lead fumes or as finely divided particles in suspension in the air. The industries, by virtue of the materials and methods they employ, are responsible for most cases of modern lead poisoning. Because quantitatively and *qualitatively, respired lead produces poisoning far more readily* than that taken in through ingestion or cutaneous absorption, most poisonings occur in industries and trades in which lead is fumed or dusted in the air. While the solubility of lead salts in the various fluid constituents of the body may have considerable bearing on certain phases of the whole aspect of lead poisoning, this chemical consideration is not so great as the portal of entry and the physiologic and metabolic activities of the poisoned organism.

Almost any of the lead salts, vaporized or in finely divided form may be absorbed from the respiratory tract. It has been found that highly significant amounts can be absorbed from the nasal mucosa *where it has been filtered out of a dust-laden atmosphere or can* be taken up from the mucosal lining of the upper and lower respiratory structures. Evidence has accumulated to show that more lead can be absorbed from the respiratory tract than from the digestive tract when each has been subjected to the same dosage, and that lead entering directly into the general circulation is more likely to produce poisoning than that passing through the portal system.

Lead is carried in the blood stream as the insoluble triple phosphate and is stored largely in the bones. Although the complete mechanism of lead storage and release is not known it has been shown to be intimately related to the hydrogen-ion concentration of the plasma and the metabolism of ionized and non-ionized calcium. Repeated dosages of lead result in its accumulation in the bones from which it is eventually released. This liberation of stored lead may occur with all degrees of speed and dosage; it may be *liberated in small inconspicuous amounts over long periods of time* so that the amount of circulating lead at any one time produces no evidences of poisoning, or it may be freed from the bones in "spurts" and produce symptoms or demonstrable laboratory findings. Alcoholic overindulgence, overfatigue, deficient calcium in the diet, are a few causes believed to precipitate mobilization of stored lead.

Elimination of lead is largely by way of the intestinal tract, all parts of which share in its excretion. The liver is an especially active eliminative organ, and when lead is ingested, this organ acts as the great bulwark against the entrance of the poison into the general circulation.

The different susceptibilities to lead found among individuals probably rest on physiologic conditions related to calcium metabolism, gastro-intestinal states, hydrogen-ion concentrations, biliary

activity, growth, other forms of intoxication such as alcoholism, and diet.

Depending on the circumstances of its absorption and storage lead poisoning may be either acute or chronic. The acute form is seen more commonly in new-comers to the trade who have received a first large dose by way of the respiratory tract. The symptoms are referable not to the portal of entry but to the gastro-intestinal and nervous systems. Constipation or enteritis, acute and colicky in nature may be the first manifestation. The central nervous system may show early involvement with epileptiform attacks, severe headache, delusions, delirium to the point of maniacal severity and blindness. An acute anemia frequently accompanies this severe form.

In the chronic forms of plumbism the classic syndrome of blue line on the gums, lead palsy, constipation, colic, anemia with stippling of the erythrocytes and blood-vessel changes are consistently found.

With the possible exception of direct nerve tissue damage as seen in lead neuritis, the most far reaching dangerous effect of continued small doses of lead is on the arterial system. This is of the nature of a progressive mesarteritis of the small arterioles which terminates in degenerative and hyaline changes and obliterative endarteritis. When the vessels of the brain are involved the manifold forms of lead encephalopathy may result; in the kidneys it produces the familiar contracted kidney. Blood-pressure is secondarily elevated and alterations of this pressure of transient nature may account for further disturbances of cerebral function.

Apart from poisoning produced from volatilized lead itself several of its salts are in common use in the industries and readily form fine respirable dusts:

Lead carbonate, "White lead," "flake white," "mineral white."
Lead acetate, "Sugar of lead."
Lead sulphate.
Lead sulphide.
Lead chromate.
Lead monoxide, "Litharge."
Lead dioxide, "Red lead."

An exhaustive survey of the occupations and trades in which lead and lead dust may become a menace to workers is beyond the scope of this work. For detailed information the reader is referred to Dr. Alice Hamilton's, "Industrial Poisons in the United States." An indication of their wide variety and nature may be seen in the following condensation of the list of lead trades given by Dublin and Leiboff in Bulletin No. 306, Bureau of Labor Statistics.

Acid finishers, amber workers, art-glass workers, artificial flower makers, bench molders, blacksmiths, blooders (tannery), book-

binders, bottle cappers, brass founders and polishers, brick burners and brick makers, bronzers, brush makers, rubber buffers, enamel burners, cable makers, color makers, compositors, cut-glass workers, cutlery makers, diamond polishers, dye makers, dyers, electroplaters and typists, emery-wheel makers, file cutters and filers, galvanizers, workers in glass, gold refiners, grinders in metals and rubber, riveters, incandescent lamp makers, jewelers, junk metal refiners, lacquer makers, lead burners, lead foil makers, lead miners, lead salts makers, linoleum makers, linseed oil burners, watch factory workers, mirror silverers, musical instruments makers, nitric acid workers, nitroglycerine makers, painters, paint makers, paint removers, paper-hangers, patent-leather makers, petroleum refiners, photograph retouchers, pipe fitters, plumbers, printers, putty makers, red-lead workers, roofers, screen workers in lead and zinc smelting, sandpaperers in enameling and painting auto-bodies, sheet metal workers, shellac makers, shot makers, solderers, steel engravers, sulphuric acid workers, tanners, temperers, tile makers, tin foil makers, tinners, toy makers, tree sprayers, type founders, welders, white lead workers, wood stainers, zinc smelters. Of recent origin is the use of tetra-ethyl lead in the automotive industry. Realizing that this compound was potentially capable of producing poisoning, a special committee was formed to investigate its harmful effects. The committee endorsed the following conclusions[1] based on the work of Dr. Leake of the United States Public Health Service:

"1. Drivers of cars using ethyl gasoline as a fuel and in which the concentration of tetra-ethyl lead was not greater than 1 part in 1380 parts by volume of gasoline showed no definite signs of lead absorption after exposures approximating two years.

"2. Employes of garages engaged in the handling and repairing of automobiles . . . . may show evidence of lead absorption and storage. . . . *In garages and stations in which ethyl gasoline was* used the amount of apparent absorption and storage was somewhat increased but the effect was slight in comparison with that shown by workers in other industries where there was a severe lead hazard (Group E); and for the period of exposures, studies were not sufficient to produce detectable symptoms of lead poisoning.

"3. In the regions in which ethyl gasoline has been used to the greatest extent as a motor fuel for a period of between two and three years, no definite cases have been discovered of recognizable lead poisoning or other disease resulting from the use of ethyl gasoline.

"In view of these conclusions your committee begs to report that in their opinion there is at present no grounds for prohibiting the use of ethyl gasoline of the composition specified, as a motor fuel,

[1] Jour. Indust. Engin. Chem., **18**, 193, 1926.

provided that its distribution and use are controlled by proper regulations."

Fatal cases of poisoning by tetra-ethyl lead have occurred at the plants where it was being manufactured. These were not entirely due however to inspired lead as this product is readily absorbed through the skin.

Due to the widespread use of lead and lead products bizarre examples of lead poisoning will continue to occur. One instance, now become familiar, was the simultaneous lead poisoning found among negro children of families who had been burning discarded electric battery boxes for stove fuel.

Physicians must keep continually on the alert for similar happenings. Technologic processes involving lead and its derivatives will continue to produce unsuspected poisonings. The only safe way in which severe poisoning and even deaths from these advances may be anticipated is through the activity of the medical profession in advising on all processes involving toxic lead preparations and in recognizing the earliest cases by foreknowledge of their possible effects.

Nickel Carbonyl ($Ni(CO)_4$).—Nickel carbonyl is a straw-colored liquid which volatilizes at room temperature. It is therefore met with ordinarily in the gaseous state in which it is inhaled.

Nickel carbonyl is a combination of nickel and carbon monoxide and dissociates at a temperature of 150° C. with the liberation of carbon monoxide and deposition of metallic nickel.

The pathogenesis of poisoning from this substance has not been determined. Armit believes that it is the result of the deposition of nickel as a slightly soluble compound over the entire respiratory surface from which it is absorbed by the tissue fluids and carried to tissues where it has a selective action, namely capillary endothelium and more especially the capillaries of the brain and adrenals where it causes hemorrhage.

On the lung itself it causes a reactionary edema and congestion.

It is eliminated through the intestinal mucosa and the kidneys.

Nickel carbonyl poisoning is limited to workers in the Mond process for the purification of nickel. In this process nickel is deposited in a finely divided state by heating the gaseous compound to the point of decomposition.

Phosphorus (P).—Phosphorus in the form of white phosphorus is the only state in which it is poisonous. This is the substance used in the old style strike-anywhere matches. The use of this substance in the manufacture of matches has been outlawed by every government, the United States having taxed it out of use in 1909. (Esch Law.) Phosphorus sesquisulphide is now used in its place and this is non-poisonous.

White phosphorus volatilizes at room temperature giving off

fumes of phosphorus and phosphoric oxide. These have a peculiar softening effect on the teeth which undergo caries and ultimate destruction. When the phosphorus reaches the periosteum of the alveolar processes it produces a proliferative reaction with swelling of the bone and the overlying soft tissues. This is the true state called "Phossy jaw." If soft tissue necrosis reaches the periosteum bacterial invasion consistently follows with the development of a severe, intractable and painful osteomyelitis and ulcerative necrosis of all tissues around the area. Systemic invasion with septicemia may follow. In some instances all of the bone of both jaws may become involved.

With the advent of the non-poisonous sesquisulphide and the red amorphous phosphorus which is used in the manufacture of safety matches, phossy jaw has disappeared from the match industry. The only other products in which white phosphorus is used are *some fireworks and incendiary bombs. Only 2 or 3 known cases of* phossy jaw from these causes are recorded from all countries.

Thiele[1] reports the only instance of death from known phosphorus poisoning in recent years. Three out of 4 persons accidentally exposed to spontaneous fumes of phosphoretted hydrogen generated from spilled wet ferrosilicon died in their apartment over the storage place where the ore had been dumped.

Hamilton states that although no cases of phosphorus poisoning have occurred in America in the making of phosphor-bronze this process is potentially dangerous. She records the finding of one case in an Austrian phosphor-bronze worker. Moreover, analysis of bronze in use in this country shows a content of 0.168 to 0.813 per cent phosphorus and the Austrian case occurred in working a metal of 0.78 per cent.

Selenium (Se).—Although the number of cases of poisoning from selenium fumes is small it is a distinct occupational hazard. Selenium is used to whiten glass and in the manufacture of ruby glass. Selenic sulphate in dry powdered form gives off fumes when melted. These affect the nose and throat in a manner described as similar to a "rose cold." Absorption of the element apparently takes place for general symptoms such as abdominal pain, vomiting and lumbar cramps have been reported. There is a characteristic garlicky taste which persists for a long period of time. This is caused by its conversion in the body to methyl selenide.

Selenium may be an impurity in copper ore and Hamilton has traced several cases of poisoning in copper works due to this source.

Tellurium (Te).—Tellurium, like selenium, is used as a reducing agent in the manufacture of colored glass and is also found as an impurity in copper and lead ore.

Telluric and tellurous oxide fumes may be inhaled in minute

[1] Thiele: Zentralbl. f. Gewerbehyg., 9, 91, 1921.

quantities and yet produce evidence of its presence in the body by the odor of methyl tellurid on the breath. Shie and Deeds[1] report the case of a man who spilled tellurous oxide and scraped it up on a piece of paper without allowing his fingers to touch it. He apparently absorbed some of the oxide through his respiratory tract for he had a garlicky odor on his breath for over a week and a metallic taste in his mouth for two days.

Absorption of larger amounts of tellurium result in diminished gastric secretion and suppression of sweat. The methyl tellurid is constantly present in the saliva, sweat and urine of poison cases.

Occasion for poisoning has been reported by Shie and Deeds in an electrolytic lead refinery where tellurium was present as an impurity in the ore. These authors predict a greater incidence and more severe form of poisoning from tellurium in the future because of its growing use in industry.

Brass.—Brass founder's poisoning, called brass founder's ague, is due to the inhalation of the fumes of zinc contained in this alloy. Pure brass poisoning, when not complicated by lead absorption due to the presence of this element in brass alloys, is in reality a zinc poisoning. It may be met with in a few trades other than those handling brass, in which zinc is an important ingredient of the materials. The copper content of brass alloy is believed to be inert insofar as poisoning is concerned.

Controversy still exists as to the nature of this form of poisoning. Repeated animal and human experiments have failed to produce the symptoms of brass founder's ague by either the inhalation or ingestion of zinc oxide powder. Drinker[2] is of the opinion that it is only the freshly formed zinc oxide from volatilized zinc which can produce this form of poisoning. The possibility that it may be due to traces of lead, arsenic or cadmium in the materials has apparently been ruled out. Drinker's explanation is based on the physical characteristics of newly formed zinc oxide, in which the particles are finely powdered and dry in contrast to the larger, more sticky particles of old zinc oxide powder. This he believes facilitates absorption by the pulmonary epithelium. The inhalation of brass fumes produces irritation of the throat and trachea and a painful cough. The ague occurs after absorption and has very much the appearance of a bacterial infection with chill, fever, sweating, and prostration. Zinc can be recovered from the feces and occasionally the urine.

Poisoning can occur in any industry where brass is melted or

[1] Shie, M. D, and Deeds, F E: U. S. Pub Health Serv., Pub. Health Rep., p 35, April 16, 1920, p 939, November 16, 1920.

[2] Drinker, P Jour Indust. Hyg., 4, 178, 1922.

zinc is volatilized. The most common process is in brass molding, the fumes being given off in dense quantities from the brass ladles and molds. Zinc smelters are exposed to similar large quantities of the fumes. Individual workers may be exposed to smaller amounts in fusing and soldering brass, especially when they must be close to their work over benches and blow pipes.

Galvanization of zinc may give off fumes if the zinc bath is allowed to get hotter than necessary.

Many industrial physicians believe that there is an immunity in *some workers to zinc poisoning. This is an observation which has* not yet been confirmed. There is undoubtedly a wide variation in the susceptibility of workers but this may be due to many factors not involved in immunity.

CHAPTER XIV.

THE DEFENSE AGAINST NOXIOUS GASES AND FUMES.

IRRESPIRABLE and poisonous gases originate from two main sources: (1) Their deliberate manufacture in industry or in industrial processes in which the materials from which they are evolved are in use; (2) generation from natural processes or as cosmopolitan poisons from substances in common use.

1. **Industrial Sources.**—Against those of the first category it is possible to apply all of the knowledge of industrial and chemical engineering and industrial medicine. As scientifically planned as the chemical industries may be today, many of the individual processes employed are obsolete. Conservatism, ignorance and economy are the basis of most failures to improve conditions of manufacture in the face of widespread propaganda for safety-first measures.

Accidents will always happen, but there can be little excuse for those responsible for the safety of workers not to anticipate breakdowns and leaks and be prepared for them.

In the United States, government regulations, recommendations of the Bureau of Mines, and Trade Unions are outstanding instruments through which safety measures can be encouraged or enforced. The average worker may be unable thoroughly to understand the particular hazards under which he is required to work but he can readily be taught that a preventable danger exists. With this knowledge of his risks he can force improvement in his condition, or accepting the risk, demand compensation.

A striking example of the effectiveness of government intervention on behalf of the worker is the passage of the Esch Law, which effectively taxed white phosphorus out of the match industry. Expediency then forced the use of the non-poisonous sesquisulphid of phosphorus which was already in use in other countries.

The Bureau of Mines has spent countless sums in the study of the mining and ore industries and presented these occupations with many practical measures and devices to prevent accidents and poisoning.

The use of tetra-ethyl lead in motor gas attracted the attention of the United States Public Health Service and a special committee was formed to study the possible danger of this material to the garage worker and private citizen; carbon monoxide studies have

been conducted on the busy streets of large cities to find out whether the man on the street was being subjected to slow poisoning from automobile exhausts; scores of municipal ordinances are in effect to control gas and fume nuisances and illuminating gas distributors are required under sanitary codes to add a characteristic odorant to their product.

Of greatest value in prevention are the improvements in machinery and methods; new-type stills; the use of high temperature glass in crucibles and retorts; electric, in place of gas and coke furnaces; automatic dumping, pouring, ladling and cleaning devices; modernized shops with good ventilation under all weather conditions; individual hoods with blow or exhaust fans over tables, benches and open furnaces; collection and condensation chambers for by-product reclamation, re-use or disposal; air filters, dampeners and washers; various forms of chemical processes by which free gases are combined and rendered innocuous; improved building materials which will not retain or absorb volatile chemicals.

As a result of these advances, the modernized chemical plant is a comparatively safe place in which to work. The writer, in visiting one of the largest plants in America in which some 150 by-products of oil were being made, was unable to detect, by odor, the building in which chlorine was produced at the rate of many gallons daily. The industrial physician at this plant stated that the treatment of poisoning from the many forms of gas generated there was almost negligible.

Unfortunately, such ideal conditions do not exist generally, and accidental deaths from absorption of poisonous gases in the United States amounted to 1695 in 1934.

In the absence of effective central control the burden of reducing accidental poisonings must rest on those directly concerned in the industries involved. That is, industrialists must keep up to date with materials and methods; industrial chemists and engineers must give full consideration to the safest methods available; the employee must demand his right to protection and exert himself in personal prophylactic measures on his own behalf.

The individual industries in which gas hazards exist are too numerous to permit discussion of the preventive measures to be applied in each. It will suffice to call attention to certain precautions which are common to many.

Firstly, workers should be informed of existing dangers. This is humane and economical, cuts down employment turnover, and prevents loss of labor-hours and output because of sickness. The worker who knows where to look for danger can always be on the lookout for it and frequently avoid it, and be prepared to combat it when it comes.

Emergency facilities should always be at hand and every em-

ployee should be instructed as to how and when to use them. This applies especially to gas masks, for all masks are not efficient, and few workers will use them routinely with any degree of effectiveness. Their use should never be permitted to take the place of the more fundamental principle of preventing the cause for their need.

Special attention must be called to those gases and fumes which seem innocuous because they do not smell bad or irritate the nose, throat or lungs: carbon monoxide, carbon dioxide, hydrocyanic acid, hydrogen sulphide (with a low margin of safety between its detection by odor and its toxic concentration), phosgene, mustard gas, arseniuretted hydrogen, mercury, and lead. Employees engaged where these gases exist must be protected from their own self assurance, for poisoning from them may reach an overwhelming degree before the worker becomes aware of his danger.

Personal cleanliness is of no less importance to workers with some of the volatile metals than to those using materials irritant to the skin. Mercury especially may volatilize from the clothing and produce respiratory poisoning. Moreover, cleanliness of the skin although not strictly preventive, is of prime importance in aiding elimination and assuring balance of excrefory functions. It may be that a person with a healthy, clear skin is less susceptible to general poisoning by absorption through the lungs. This is a possible element in the whole involved subject of tolerance.

2. **Natural and Cosmopolitan Sources.**—The gas poisons of the second group are hazards to the general population. They consist of carbon monoxide, carbon dioxide, hydrogen sulphide, ammonia, lead and the war gases. Owing to their origin at times under the most innocent or unsuspected circumstances, deaths due to them are frequent and often unexplained. On the other hand, familiarity with their poisonous effects has resulted in the use of some as suicidal and homicidal poisons.

The only effectual measure against this group is education. No child should be permitted to go in ignorance of the fact that illuminating and stove gas is dangerous; every boy and girl in the grammar school grades should know why a flame will go out if it is lowered into a deep well; adults should know enough simple chemistry to understand why sewers sometimes blow up, and why it is dangerous to go down into man-holes and similar places where organic gases can accumulate; and young and old alike can understand the danger of warming up the autmobile in a closed garage.

Every open fire should be considered a potential danger from carbon monoxide. That more poisoning from this source does not occur is due to the manner in which stoves and flues are built. But faults may develop; the flue may become clogged with soot or it may have been closed off deliberately and not reopened when the fire was started again. Many grates and fireplaces in cheap dwellings

may be passed on as safe insofar as fire hazards are concerned, but remain as efficient poison-gas generators.

Banked fires and smoldering dump fires are especially dangerous and should not be permitted for any length of time.

Carbon monoxide is the dangerous ingredient of illuminating and cooking gas. Its entrance into dwellings is always through mechanical fixtures, and these are not always perfect and accident-proof. Old stoves and light-brackets become worn and rusted and thereby liable to leaks. A pet-cock may become so loose as to be turned on accidentally by the slightest touch. Inspectors and underwriters should be diligent in their search for existing faults of this kind.

The common habit of leaving a gas jet turned low as a night light is exceedingly dangerous, for a light draught or sudden wind may extinguish it and permit the free gas to pour into the room; or the pressure in the gas mains may fall to such a point as to put out the light and on the return of pressure the gas will then flow again, unignited. If the habit of keeping a night light is to be practised there should always be a partially opened window in the room, but not so near the light as to permit it to be blown out.

Carbon dioxide may be generated wherever organic material is decomposed. Most of the innocent, non-industrial poisonings from this gas have occurred through ignorance of the fact that old leaves and refuse, organic dusts, silage, dead animal products, and coal give off carbon dioxide when they decompose or rot, and that if this occurs in unventilated, closed spaces, the gas may accumulate there in poisonous amounts.

Hydrogen sulphide gas is often responsible for poisoning in confined spaces where there is decomposing organic matter. Although the characteristic odor of rotten eggs is warning enough in high concentrations only 2 or 3 parts per 1000 of air may prove fatal. When conditions exist where hydrogen sulphide and carbon dioxide are both being formed, the oxygen content of the air is greatly reduced and overwhelming asphyxia may be sudden and fatal. It is largely because of this combination of gases that all sewers and drains are vented. Unskilled workmen should not be permitted to enter closed sewers, old vats or long-closed earthen cellars without having first taken the precaution to see that they are aërated. For the same reasons farmers should be warned against entering silos before airing them.

The dangers from automobile exhausts is great where it is necessary to heat up a cooled engine in the garage before taking it out. Under the discussion of carbon monoxide (p. 137) it was shown how rapidly this poison may accumulate to dangerous proportions from an engine running at idle in an average garage without ventilation. Every car-owner should be made cognizant of this fact.

Acute poisoning from ammonia gas may result from the use of

nicotine. It is absorbed from the respiratory epithelium and enters directly into the blood stream. Taken through this avenue it is possible that a given dose may be more toxic than a similar amount absorbed from the digestive tract because the latter is required to pass through the liver.

According to Haggard and Greenberg,[1] the physiologic effects of nicotine absorbed from the respiratory tract are elevation of blood-pressure, increase in pulse-rate, increase in blood sugar and respiratory quotient, and lowering of skin temperature in the extremities. Evidence points to these as due to the action of nicotine on the sympathetic nervous system and adrenals. "Tobacco heart" is explained by the same mechanism. Doubt has been thrown on previous assumptions that nicotine affects the heart muscle directly. Laubry, Deglaude and Walser[2] conclude that small and moderate doses of nicotine, corresponding to the amounts absorbed by an average smoker, produce vaso-dilation, while stronger and continued doses produce weak vaso-constriction. The latter is the common finding in most recent investigations. The correlation of these effects with the symptoms ordinarily ascribed to tobacco smoking are undoubtedly significant. The dizziness, headache, palpitations, nausea, flushing, and tingling in the fingers are all prone to be evanescent, irregular and non-predictable and it is difficult to know what accounts for their presence or absence in any particular case.

It is common experience for some of these sensations to be felt by inveterate smokers. It is probable that the habituated smoker does not ordinarily feel these effects because he unconsciously controls the dosage which he permits himself at any one time. The assumption is that these symptoms are real effects of nicotine absorption, but that the experienced smoker subconsciously feels one or more of them to an uncomfortable degree and temporarily loses his "desire" for smoking. He then either crushes his cigarette out or refrains from smoking until the effects of the last smoke have passed off. This theory has the necessary correlations with the facts of common experience.

Cushny is of the opinion that the nausea and abdominal symptoms of tyros in the art of smoking are due to stimulation of the motor ganglia of the intestinal wall, which leads to exaggerated peristaltic contractions and later intestinal paralysis. The fact that these symptoms are usually associated with beginners and are seldom seen in long habituated smokers has been used as evidence of a developing tolerance. It may be due only to inexperience in its use, since some experienced smokers develop real abdominal cramps after excessive indulgence. The loss or reduction of appetite attrib-

[1] Haggard, H. W., and Greenberg, L. E.: Science, 79, 165, 1934
[2] Paris letter Jour. Am Med Assn, 101, 3, 458, 1933.

uted to smoking is explained by Haggard and Greenberg[1] as due to *the elevation of the blood sugar level which temporarily reduces* tissue needs, and therefore hunger. Friedrich[2] states that nicotine produces hyperchlorhydria by increasing gastric secretion.

Those who accept tobacco amblyopia as a reality, explain it on the probable effect of nicotine on the postretinal ganglia, or the retinal or optic vessels.

Although nicotine is known to have a vaso-constrictor effect it has not been proven that smoking is primarily concerned in the etiology of arteriosclerosis, endarteritis obliterans, atheroma, Raynaud's disease, or angina pectoris as has been claimed by some. It may aggravate these conditions, however, by adding its vaso-constrictor effects to those already existing in these conditions. But the most cautious students of the subject refrain from denying the possible harmful effects of smoking in individuals who have any conditions manifesting impaired circulation. Ochsner, Gage and Hosoi[3] believe that tobacco smoking may be one contributory factor in the development of peptic ulcer in individuals who have an ulcer predisposition.

Tolerance to tobacco resolves itself at present to accustomedness to its use and the control of disuse. In explanation of apparent intolerance there is the possibility that there may be an individual susceptibility to absorbed nicotine since sensitivity to it by skin contact has been shown to exist in some persons. Susceptibility may be only another way, however, of expressing hyperirritability of the autonomic nervous system.

Snuff is powdered tobacco. It is weaker than smoking tobacco and the amount of nicotine absorbed by its inhalation through the nose is probably small. Its continued use may give rise to catarrhal conditions of the nasal mucosa.

Opium.—Opium is smoked for the effects of its main alkaloid, morphine. The use of the drug in this form is still practised generally *in those countries in which it has long been a national habit.* It was also smoked in the occidental countries when it was first introduced to them, but this method has been almost completely replaced by the use of opium preparations by mouth or injection.

As prepared for use in the pipe, opium is a thick, inspissated mass obtained by infusing, washing and evaporating the juice of the poppy plant, *Papaver somniferum.* It still retains the phenanthrene alkaloids, morphine, codeine and narcotine, but the isoquinoline *alkaloids have been separated out with the resins, caoutchouc, fats* and oils. Morphine taken in this way has none of the bitter taste of the alkaloidal salts, and this fact combined with the aromatic

[1] Haggard, H. W., and Greenberg, L. E. Science, 79, 165, 1934.
[2] Friedrich, R.. Arch. f. klin. Chir, 179, 9, 1934.
[3] Ochsner, A., Gage, M, and Hosoi, K. Surg, Gynec and Obst, 62, 257, 1936.

line nitrites and the loss of the amyl radicle through oxidation. The nitrites are eliminated in the urine as such or are first oxidized to nitrates and then eliminated.

Ether.—Absolute ether is ethyl oxide. Commercial sulphuric ether is 96 per cent by weight ethyl oxide and 2 to 4 per cent alcohol. It is the latter that is used as an anesthetic. Sulphuric ether is highly volatile, colorless, heavier than air, and inflammable.

Concentrated ether vapor is highly irritating to the mucous membranes of the respiratory tract and when inhaled too quickly causes spasmodic arrest of respiration. For this reason it is generally administered slowly, allowing it to mix with air, or oxygen is given along with it.

The amount of ether that enters the circulation from the alveoli is dependent upon its partial pressure; *i. e.*, the balance between the ether concentration in the alveoli and in the blood. An excess on either side causes its passage toward the lowest concentration. Forced anesthesia can therefore raise the concentration in the lungs to a point that will bring the amount in the blood to dangerous proportions. Conversely, to allow the air or oxygen to enter the alveoli, or to force the ether out of the lungs by artificial respiration will permit passage of the ether out of the blood.

Ether is primarily a depressant of the sensory side of the brain, medulla and spinal cord. Increasing concentration depresses the motor tracts and motor side of the medulla. Its action on the nervous system is probably a simple chemical reaction with cellular constituents, most likely the lipoids, and a temporary inhibition of their functions. Hare states that the diaphragm is the first part of the respiratory mechanism to yield to respiratory paralysis and observation of this organ during anesthesia is as important as watching the reflexes and respiration. Death from overdosage of ether is due to paralysis of the respiratory center.

Anoxemic symptoms such as cyanosis, jugular pulsation, and general circulatory failure, should not be confused with those due to ether.

Ether does not have any damaging effect on normal kidneys but may produce suppression of urine in nephritic subjects. The tendency of ether to cause acidosis makes it a dangerous drug to use in the presence of diabetes mellitus unless it is employed in light amounts.

The nausea and vomiting after ether are frequently the result of its improper use. Careful administration at the beginning, the prevention of overconcentration at all times, and judicious admission of air and oxygen toward the end of anesthesia should reduce the after effects to a minimum. Postanesthetic ileus is more often due to faulty preparation for anesthesia and poor surgical technic in abdominal operations than to ether itself. Ether is contra-

indicated, or to be used very cautiously, in the presence of bronchitis, pulmonary tuberculosis, nephritis and diabetes. It is dangerous in subjects with arteriosclerosis and aneurism.

Chloroform ($CHCl_3$).—Chloroform is a highly volatile liquid with a sweetish characteristic odor. It is non-irritating to the respiratory passages. Its absorption and elimination by the lungs is, like ether, dependent on the partial pressure of the gas in the alveoli and lung capillaries. Absorption of dangerous amounts is enhanced by the use of the "closed method" that is its administration with little air or oxygen. Elimination is favored by any measures which hasten its removal from the alveoli.

Chloroform acts intracellularly on nerve cells by entering into chemical change with the cell lipoids. It first produces loss of consciousness by its effect on the higher brain centers and subsequently depresses the sensory and motor sides of the brain, cord and medulla.

The most *immediate toxic effect of chloroform is on the circulatory* system. It is a direct poison to the musculature of the heart and blood-vessels. As a result, the heart beat weakens, the ventricles come to a standstill in diastole, and the vessel walls dilate. Together these effects can lower the blood-pressure to a fatal degree.

Chloroform also produces anoxemia by reducing the oxygen-carrying capacity of the red blood cells.

Chloroform is a metabolic poison as shown by the production of fatty degeneration of the liver, kidney and heart. This may occur after a single dose, but more frequently follows repeated administrations.

Acetonuria and glycosuria are often seen after chloroform, probably the result of liver damage. It is therefore a dangerous anesthetic for diabetic subjects.

Nitrous Oxide.—Nitrous oxide (N_2O) is a non-irritating anesthetic gas widely used for minor operations and in dentistry. Recent apparatuses for its administration have been so perfected that control of the dosage and admixture with air or oxygen make it possible to use nitrous oxide for prolonged anesthesia.

It is absorbed through the alveolar epithelium and carried in simple solution in the blood.

The action of nitrous oxide is two fold; it has a specific effect on nerve tissue, and as an inert gas produces anoxemia by exclusion of oxygen. On the brain, it acts by chemical reaction within the cells.

Pure nitrous oxide produces rapid and fatal anoxemia. There is early cyanosis, deepened respiration, slowing of the pulse and elevation of the blood-pressure. Admixture with oxygen diminishes these effects in direct proportion to the amount of oxygen used. For effective anesthesia without anoxemia a mixture of 92 or 93 per cent nitrous oxide with 5 to 7 per cent oxygen is found best. There

is a wide margin of safety between the concentration necessary for anesthesia and that which will cause death.

Nitrous oxide is not a tissue poison for its use results in no after effects. A harmless symptomatic glycosuria may appear temporarily after its use.

Many warn against the use of nitrous oxide in cardiac cases because it increases blood-pressure but this seems to be an unwarranted fear for no serious elevation of blood-pressure will occur if the anesthetic is properly mixed with oxygen and the mixture is carefully controlled throughout.

Ethylene.—Ethylene (CH_2—CH_2) is a gas at ordinary room temperatures. It is supplied for anesthetic purposes in compression cylinders.

As used at present in a mixture of 90 per cent ethylene and 10 per cent oxygen, it is the most satisfactory general anesthetic. Absorption and elimination appear to be entirely through the lungs. Its only important physiologic action is its inhibitory effect on, first the sensory, and then the motor sides of the brain.

A slight fall of blood-pressure of 10 to 15 mm. may occur after its prolonged use. It is non-irritating to the air passages and produces no anoxemia.

The only apparent danger connected with the use of ethylene is its explosive character when mixed with air. This can occur most readily when the ethylene constitutes between 75 per cent and 25 per cent of the mixture. Ignition from static discharges in the anesthesia apparatus has occurred.

PREVENTION OF POISONING BY INHALED DRUGS AND ANESTHETICS.

Drugs acquired by inhalation are taken deliberately for personal gratification, for use as medicine, with suicidal intent, or are administered as medication, anesthetics or homicidal agents. Prevention of intoxication from this class of poisons must consider their availability to the general public and the factors that influence their use or abuse, and must recognize the dangers in their administration for medical purposes.

Tobacco, opium and cannabis must be looked upon as social poisons. While their use is intentional and individual they are important factors in the social life of the community and their existence there as potential poisons is of great importance to public health. Unfortunately, the concern of society regarding them is not so much with their health aspects as with the economics of their production and distribution.

Opium is primarily an Old World drug and tobacco belongs to the New World. The interchange of these two drugs between the East

and the West has been the most important factor in the degradation that accompanies their use. Opium, as smoked in China is relatively harmless compared to the way it is used by the degraded unfortunates of Western society, and tobacco as formerly used in moderation and by a few in Europe and the Americas, was much less of a health menace than its present use by both sexes, and all ages in the Far East.

It can be admitted as proven that tobacco is a potential poison. One of the most remarkable phenomena of the present day is the almost unquestioned acceptance by society of a poison such as nicotine. Propagandist advertising has turned an unhygienic vice *into a twentieth century virtue. No regard whatever is given to the* potential health hazards of tobacco abuse, apparently reflecting the assumption that it is not abused. Tobacco smoking is an acquired habit, continued in most cases in spite of a disagreeable, if not stormy introduction to its use, and the admission by most smokers that there are times when they wish they could give it up. Physicians in general have no clear-cut opinions about tobacco smoking. They base their judgments largely on empiric observations on their smoking patients *and friends, accepting subjective opinions about* it from others and tincturing their own judgment with their personal prejudices for or against it.

The writer is convinced that there is sufficient evidence to brand tobacco as a poison for the great majority of users, for the habitual smoker repeatedly abuses it. Accepting what is known about tobacco preparations as they are smoked today and the physiologic effects of nicotine as they have been presented, it is imperative that doctors safeguard the public health by sound advice about smoking and by counter-propaganda to that which proclaims its harmlessness and virtues.

This must be done against advertising which presents only the esthetic sides of smoking and the qualities of the various brands, and the insinuations of their harmlessness in the testimonials of famed athletes, singers and social, business and intellectual personages.

Instead of deploring the use of tobacco entirely, or commending it for its soothing effect on jangled nerves, or simply condoning it, *the physician should exert his influence toward impressing the would-*be smoker with the fact that he is about to take up the use of a potentially harmful drug. He should teach moderation; interdict it when necessary on medical grounds; advise and instruct on the possibilities of intoxication by abuse, or hypersensitivity to tobacco.

Legal measures to prohibit the sale of tobacco to minors have been forgotten in the current wave of unprecedented sales. It is likely that these laws if enforced would have little effect in view of the ready availability of cigarettes from private sources and the

lack of any united public opinion against their use by young people. Much has been said about the effect of tobacco on adolescents but no reliable evidence is at hand to show that it is more harmful during the growing period than after maturity.

In conclusion, the prevention of tobacco poisoning is the prevention of nicotine intoxication. Since this latter occurs to any appreciable extent only in exceptional circumstances attendant on its use and is not an inevitable concomitant of smoking, prevention is simplified for the individual by rational control or the acquisition of good habits of use. Predisposing factors such as nervousness, worry, restlessness and the satisfaction obtained from the associated automatic movements, such as rhythmic movements of the hands, lips or jaws which smoking brings about, are all to be taken into consideration in attempting to control the extent to which an individual smokes and his liability to intoxication. These are psychic factors which are amenable to control and their control should go far toward preventing tobacco poisoning.

Opium and cannabis smoking can be considered together because they are both employed in the same way for the same purpose, that is, for their narcotic effect. This precludes their casual use throughout the day and during working hours and limits them to periods of idleness. They are therefore intimately bound up with the life and customs of the people, or to deliberate addiction to them at the expense of other activities. Thus, in the Far East, opium smoking is the customary enjoyment of after-working hours of many, while in the West its use is largely restricted to narcotic habitues.

International agreements regulating the opium trade are the broadest measures taken against the widespread use of this drug and national laws have served well to regulate its availability in limited communities. The Commission on Opium Traffic of the League of Nations has been the potent instrument in world-wide control and Federal and State Narcotic Laws have restricted its use in local areas. There is strong reason to believe that these efforts are born more of economic than health reasons. In the United States the unlicensed possession of opium or marihuana is a punishable offense—it is not necessary that the possessor have it for sale.

Opium smoking has never become a national habit in the United States and the use of marihuana has only recently come to public notice because of the increasing number of convictions obtained against its users. In the case of both drugs, it is more a matter of the types of persons who use them than a question of harm from their use. The opium and marihuana habitue is notoriously an unfortunate character, primarily a constitutional inferior or psychopathic personality, an adventurer or a coward, a sensualist, or a youthful bravado. (This does not apply to narcotic drug addicts

in general, but only to those who resort to the time-consuming method of smoking opium and cannabis.)

In the great majority of cases the use of these drugs should be looked upon as an unfortunate concomitant of more serious personality defects and because of their habit-forming nature every effort should be made to keep them out of the hands of those liable to be misled by the false hopes attributed to their addiction. The temporary pleasures accompanying their use can only be followed by further degradation brought about by acts performed under their influence, or the sly, underhand measures resorted to in order to obtain them. The most far-reaching efforts toward the prevention of opium and cannabis poisoning will always be those directed toward the welfare of their potential users. Of special importance are those undertakings that limit their availability to adventurous, weak-willed, mimicking youths, who take them first out of a spirit of bravado or because it is the "thing to do" in the company in which they are thrown.

General anesthetics administered for legitimate medical reasons act as poisons in bringing about their desired effects, but medical anesthesia keeps these effects to sublethal amounts. Any anesthetic can cause death from an overdose and it is the recognition of this possibility that underlies the prevention of accidents from them. Prevention must be based on knowledge of the physiologic effect of these profound poisons, their limits of safety and special consideration of the person anesthetized. Since the anesthetized person is unconscious, objective measures of the degree of intoxication must be relied upon. Rules of thumb are unsafe, and unintelligent. For this reason the anesthetist must have complete understanding of the technics of anesthesia and a sound medical knowledge with which to interpret untoward reactions. The anesthetist should be chosen with as much consideration of his ability as the surgeon.

For the criteria upon which one anesthetic is selected over others for different operations and in the presence of particular pathologic conditions the reader is referred to fuller works on that subject. Chloroform is the anesthetic most commonly employed for homicidal purposes. It cannot be used for suicide because the state of unconsciousness produced precludes its continued self-administration to fatal amounts. Chloroform can be purchased in the open market so there is no way to prevent its use with homicidal intent.

DUST AND AIR-BORNE PARTICLES.

(Exclusive of Microörganisms).

Moving air is the vehicle by which finely divided particles suspended in it are carried into the nose, mouth, throat and lungs. The amount and variety of such particles in a measured amount of air depends on the extent of the sources from which they originate,

the forces which propel them into the air, the physical state of the atmosphere, their size, specific gravity and surface area, the velocity of motion imparted to them from their source and the rate of motion of the air which carries them. Due to the wide variability of these factors, the number of particles per given volume of air varies greatly. Even the purest air at the earth's surface (except when deliberately purified in the laboratory) has measurable amounts of dust in it, the counts ranging from 1000 or less particles to many million per cubic liter. Their size may vary from less than 1 micron in diameter to the visible fibers of vegetable origin which may be seen floating across a sunbeam.

The human organism is therefore surrounded constantly with dust-contaminated air. Whether these foreign particles can do harm must depend on whether they can produce pathologic reactions when introduced into the body. For a given type of particle, the "dose" must also be considered, and this in turn is dependent upon the amount present in the air and that which actually reaches the tissues where the reaction occurs. Inhaled particulate matter, then, has the same criteria as other inspired poisons; *i. e.*, its physical-chemical nature and its dosage.

Within recent years almost all harmful inspired particles have come to be looked upon as chemical agents of disease. If their purely physical nature, such as hardness or roughness is responsible for harmful effects it is probably so to a very slight extent. On this assumption an inhaled particle which has the power of producing harm does so by entering into chemical or physico-chemical reaction with the body tissues; those substances which gain entrance to the respiratory system and do no harm are chemically inert and are disposed of by normal defense processes of the body. In this latter instance the pathologist may demonstrate local tissue reactions but these do not imply disease—they are morphologic evidences of the ability of tissues to react within their limits of tolerance.

The first defense of the body against dusts is the filtering power of the nose. This is effected by the presence of hair in the external nares and the large moist surface of the internal structures of the nose. Lehmann[1] finds wide variation in the efficiency of this mechanism. He has demonstrated that some nares filter out more than 70 per cent of a measured amount of dust and others are hardly able to remove any of it.

The column of air which passes through the nose strikes the moist mucous membrane lining the naso-pharynx and pharynx. Here more particulate matter is removed by the sticky mucus. The same holds true for the lining of the trachea and bronchial tree. Disposal of the impinged particles is by discharge of mucus from the nose, the swallowing of pharyngeal mucus mixed with saliva, the outward motion of the bronchial ciliated epithelium which

[1] Lehmann, G · J. Indust. Hyg., 17, 37, 1935

carries the mucus to a position from where it can be coughed up, and the action of phagocytes which take up particles that have reached the lung tissue proper.

Probably a very small percentage of foreign particles ever reach the lung tissue. Adelaide Smith estimates that silica particles of more than 10 microns in their greatest diameter never do so.

Foreign particles suspended in air originate from two sources or circumstances of origin:

1. Cosmopolitan sources.
2. Industrial sources.

Cosmopolitan Dusts are complexes of organic and inorganic materials made up of mineral débris from the earth's crust, finely divided or powdered vegetable matter and pollens, and particles of animal origin. The amount of inorganic elements is of sufficient volume to be harmful only under exceptional circumstances, such as during dust storms or in regions where the atmosphere is polluted by industrial plants, nearby quarries or other dust-raising activities. The lungs of most city dwellers show variable amounts of carbon and silica deposits even though these people may never have been engaged in dusty trades. Inorganic dusts breathed in under ordinary living conditions are probably harmless, at least to the lungs, but where meteorologic conditions are favorable the continuous habitation in a dusty atmosphere may result in catarrhal changes in the nose and pharynx.

Sensitization.—Vegetable and animal particles in common dusts may be distinctly harmful because of individual peculiarities in the reactions of certain people to even minute quantities of them. This reaction is known as hypersensitiveness or allergy and is a specific response of the tissues of the body to these organic substances. So far as is known, allergic response is elicited only by proteins (possible exceptions are discussed elsewhere). The undoubted chemical nature of hypersensitiveness places foreign proteins among the exogenous chemical agents of disease. Although the complete mechanism of the allergic response is not understood the initiating process seems to be cellular in origin. In the case of inspired pollens it is probably the cells of the upper respiratory tract which are first involved. Eventually, cells in tissues widely separated from those in the nose share in the ability to react to the specific protein responsible for the condition. Thus, in asthmatics the skin epithelium becomes sensitized and reacts to the specific pollen which first affected the respiratory epithelium. Many authorities believe that chemical receptors are produced by the tissue cells in an attempt to deal with the large, non-diffusible protein molecules. These chemical substances break up the complex proteins, and permit them to be absorbed but the cells remain "allergic" or *sensitive thereafter and retain the power to react* rapidly to subsequent experiences with the same specific protein

molecule. There is evidence that an aromatic carbon ring in the protein molecule may be largely responsible for the process. It is suggestive that glycerin is the only protein incapable of producing allergic response and that it contains no aromatic ring, its carbon atoms being arranged in a chain.

Below is a partial list of the sources of natural proteins capable of producing hypersensitiveness by way of the respiratory tract. They are all capable of being thrown into the air and inhaled, but their size (mostly over 10 microns) probably precludes the possibility of their reaching the lung proper.

PLANT POLLENS.

Southern ragweed—*Ambrosia elatior*
Giant ragweed—*Ambrosia trifida*
Lamb's quarter—*Chenopodium album*
Bermuda grass—*Cynodon dactylon*
Timothy—*Phleum pratense*
Red-top—*Agrostis alba*
Orchard grass—*Dactylis glomerata*
Couch grass—*Agropyron repens*
Cocklebur—*Xanthium commune*
Marsh (cord) grass—*Spartina glabra*
Foxtail—*Alopecurus pratensis*
Plantain—*Plantago spp.*
June (blue) grass—*Poa pratensis*
Sweet vernal—*Anthoxanthum odoratum*
Crab grass—*Panicum sanguinale*
Sheep sorrel—*Rumex acetosella*
Rye grass—*Lolium perenne*
Yellow dock—*Rumex crispus*
Spring (spiny) amaranth—*Amaranthus spinosus*
Hemp weed—*Cannabis sativa*
Pig-weed—*Amaranthus retroflexus*
Hop—*Humulus lupulus*
Marsh elder—*Iva frutescens*
Prairie sage—*Artemisia ludoviciana*
Annual sage—*Artemisia annua*
Brome grass—*Bromus ciliatus, B. racemosus*
Goldenrod—*Solidago memoralis*
Elm—*Ulmus spp.*
Birch—*Betula nigra*
Oak—*Quercus spp.*
Ash—*Fraxinus americana*
Pine—*Pinus spp.*
Alder—*Alnus spp.*
Lagustrum—*Lagustrum vulgare*
Cottonwood—*Populus deltoides*
Black walnut—*Juglans nigra*
Hickory—*Carya spp.*
Box elder—*Acer negundo*
Ironwood—*Ostrya virginica*

VEGETABLE DUSTS.

Teak
Boxwood
Redwood (Sequoia)
Cotton and cottonseed
Orris root
Wheat
Malt
Coffee
Flax
Jute
Rice
Corn
Kapok
Hay and straw
House dust
Arrowroot

ANIMAL PRODUCTS.

Cow dander
Horse dander—horse hair
Dog hair
Cat hair
Mouse products
Leather
Fish glue
Rabbit products
Guinea-pig products
Sheep wool
Mohair (goat hair)
Alpaca and llama hair
Feathers
Muskrat products
Mink products
Chicken feathers
Goose feathers
Duck feathers

The foreign proteins contained in these sources are called anaphylactogens. Upon their proper introduction into the animal body antibodies of specific nature (anaphylactin) are formed against them. It requires about eight days for the active production of the anaphylactic (allergic) state.

Weil[1] believes that the antibodies are fixed in the cells and it is there that the reaction with the antigen occurs.

Apparently, during the process of breaking up of the proteins by the cells, a fraction is liberated or generated, which is responsible for the clinical manifestations of anaphylaxis. This still unidentified substance is called anaphylotoxin and appears to be the same for all anaphylactogens.

On the basis of this theory there is therefore a specific reaction for each foreign protein (or at least closely related origins of the proteins) and a general reaction common to all anaphylactogens.

The most common clinical manifestations of allergy produced by inhalation of proteins are hay fever, allergic rhinitis and asthma. The seasonal incidence of these diseases is in no way related to any seasonal changes in the tendency or susceptibility to react to the antigens, but is a reflection of the time of year when their source is most abundant; *e. g.*, pollenation of early spring grass in May and June and of the ragweed in late summer and autumn. Non-seasonal asthma and other allergic diseases are due to substances commonly present the year-round, such as those of vegetable dust and animal origin.

One of the most important questions in the etiology of allergic diseases still remains unanswered. Why should only a few of all those exposed to the common sources of foreign proteins develop hypersensitiveness? The answer must rest in some unknown factor in the mechanism. Two suggestions have been made—first that there is an inherited constitutional basis for the development of allergy, and second that some pre-existing postnatal condition has altered the local resisting mechanisms in such a way as to permit large protein molecules to come into intimate contact with the tissue cells. Such conditions as catarrh or other injuries to mucous membranes have been suggested as contributing causes. It has also been postulated that exhaustion from general conditions, such as nervous shock may be a cause.

Obviously, it is important that an explanation be found for the wide discrepancy between the many opportunities for the development of hypersensitiveness and the relatively few instances in which it actually results.

Industrial sources of dust may include special opportunities of exposure to many of the etiologic factors already considered under every-day living conditions. Thus, farriers and hostlers are daily

[1] Weil, R.: *Jour. Med. Res*, 27, 497, 1913, *Ibid*, 32, 107, 1915

exposed to animal emanations; tanners, furriers and wool workers frequently work in dusty atmospheres containing hair and wool; sawyers and wood workers are exposed to the allergens in saw-dust and glue; farmers work in the dusts of hay and straw, especially during harvesting; bakers and millers breathe the dust of ground corn, wheat and rye; laboratory workers handle rabbits, mice and guinea-pigs. In these trades, as in civil life, allergic diseases are common and the same question arises as to why some react and others do not, or why some develop hypersensitiveness only after long exposure to the causative agents and others almost immediately after taking up the trade.

The importance of inorganic dusts met with under industrial conditions is in direct contrast to the part they play in exposures of every-day life. Pneumoconiosis is almost entirely an industrial disease. While it may be seen in minor or subclinical form in the non-industrial population it assumes high economic importance in the industries and becomes a real industrial hazard.

Many of the common names for diseases met with in dusty trades show this connection: "miner's phthisis;" "miner's asthma;" "stone-cutter's phthisis;" "potter's rot."

Mineral Dusts.—*Silicosis.*—Silicon is estimated to constitute one-fourth of the earth's crust. All of the sandstones, granites, clays, quartz, feldspars and micas are largely silicates. Combinations of silica with other minerals are present in the great majority of all mine and quarry products, and the vegetable kingdom contains varying proportions of silicates deposited in the fibrous materials of stems and leaves.

Opportunities for the pulverization of silica compounds are great in many of the commonest trades. In this state silicon can be inhaled, and provided the particles are small enough (less than 10 microns) can reach the terminal pulmonary epithelium. The present concept of silicosis is that of a physico-chemical reaction within the lung tissue between the soluble hydrate of silica and the alkaline solute of the tissues. It is held that carbon and clays inhibit the solubility of the hydrosol by coagulation and the formation of colloidal silicon.

Silica particles are not subjectively irritating to the respiratory membranes unless in sufficient amounts to produce choking by a cloud of dust.

On absorption in the lung tissue, silica is phagocytized and, within the cells, is carried along the perivascular and peribronchial lymphatics. In time these cells accumulate along the lymph channels and cause blockage: a productive inflammatory reaction is set up about them. Typically, the reaction is a fibrosis and appears as nodules built up in whorl-like formations which may reach several centimeters in diameter. Linear deposits and fibrosis also occur.

The fibrous tissue undergoes contraction and brings about the distortions of the lung architecture. With complete blockage of a lymph drainage system in any area the phagocytes invade the pulmonary septa and there produce similar fibrotic reactions, in this instance diffuse and tending to be widespread. All the tracheobronchial and hilar lymph nodes become involved early and show the same fibroblast response.

Central necrosis may occur in the interior of a silicotic nodule. This is believed to be due to toxic death of cells and not to deprivation of blood supply.

Fallon[1] concludes from his experimental work that the monocytes become loaded with quartz particles and that this produces disintegration of the monocytes and the discharge of their contents. The liberated silica, which he believes is practically unchanged, stimulates further monocyte response and permits a repetition of the cycle.

The length of time required for the development of silicosis appears to be determined largely by the physical conditions under which it is acquired. Of these, the most important is size of particles, which in turn is the surface area of the silica inhaled. Very finely divided particles, such as those in blast dust, present a relatively larger surface area in the aggregate than the larger dusts encountered in stone-cutting. This greater surface area enhances solution and phagocytosis. (It must be recalled that blockage of lymphatics is not produced by mechanical obstruction by silicious particles but by damaged silica-bearing cells.)

Experimental silicosis may produce demonstrable changes in three to six months. Actually, silicosis does not assume clinical importance until after several years' exposure. A rapidly developing case may appear in two years. The average exposure of silicotics has been found to be around twelve years. The rapidity of development varies with the trades in which it is acquired. Mavrogordato reports the mean duration of exposure of miners in the Witwatersrand as ten to eleven years; the British pottery industry twenty-five years; porcelain industry ten years or more; sand blasting, less than three to eight years.

Great interest is centered around the possible rôle of silicosis as a predisposing or aggravating cause of pulmonary tuberculosis. The opinion now holds that the chemical-cellular changes produced by silicosis produce a soil especially favorable to the growth of the tubercle bacillus. Most advanced silicotics have pulmonary tuberculosis and most deaths occurring in those with silicosis are due to tuberculosis. Fallon demonstrates a local increase in phospholipids in silicosis and tuberculosis which he attributes to derivation from the monocytes in the lesions in both of these diseases. Silicosis is

[1] Fallon, J. T. Canad Med. Assn. Jour., 36, 223, 1937.

now recognized as one of the most important occupational diseases. It is found most frequently in the following trades and industries:

Sand-blasting.—Fine silicious sand is blown from pneumatic blasts to wear down or polish stone and metallic surfaces. Thick clouds of sand from the blast and the material being polished surround the nozzle of the blast. A large proportion of the sand grains are less than 5 microns in diameter, due in part to repeated use of the same sand.

Granite-cutting.—A fine dust arises from the sawing and chipping processes.

Sandstone-quarrying.—One of the most prolific sources of silicosis through cutting, drilling and blasting.

Metal Grinding.—Dust produced from sandstone and other abrasive wheels.

Refractories.—Gannister and silica brick manufacturers.

Mining.—Some silica is encountered in all mines. Coal contains varying proportions of silica. Tin ores, feldspar, quartz, slate, and mixed dust from mines for precious and semi-precious stones may all yield high silicious dust. This is especially true when blasting is used for loosening.

Pottery and Enamelware.—Due to ground flint, powdered clays and feldspar. The compound dust is shaken into the molds and blown off during the firing process.

Manufacturing Scouring Soaps.

Soapstone and Talc Industries.

Tunneling and Subsurface Engineering Projects.

Grinding and Threshing of Vegetable Fibers.—Cane, cornhusk, grain and other heavy cellulose fibers may yield a fine vegetable dust containing silicates.

Asbestosis.—Asbestos is a form of serpentine. It is a hydrated ammonium silicate containing 2.6 per cent free and 44.1 per cent combined silica along with small amounts of iron and nickel.

In the mineral seam, asbestos occurs as a compact stone made up of asbestos fibers. It is obtained by blasting in open quarries. The fabrication processes for the manufacture of sheet asbestos, asbestos cement and asbestos textiles require first that the asbestos rock be crushed and teased. Opportunity for dust to arise occurs at the quarry, the crushing plant and the manufactory. The greatest hazard arises in the shaking and sorting process where the asbestos fibers are separated and handled commercially.

Asbestos owes its pathologic significance to the contained silica and asbestosis is a modified silicosis. In the fiber form it is relatively less soluble than as sand particles and its effect on the lung is more local. Absorption and phagocytosis occur, but the process of deposition and reaction remains largely around the respiratory bronchiole. In this area it produces a fibrous "cuff" without the

typical silicotic nodule. The "asbestos bodies" found in the lungs of asbestosis cases are asbestos fiber cores surrounded by endogenous pigmented materials obtained from the tissues. These may appear in the sputum and their color ranges from golden-yellow to mahogany brown.

Asbestosis does not favor the development of pulmonary tuberculosis as does silicosis. It is of itself a chronic disease which once acquired becomes permanent.

Siderosis.—The dust of iron, copper and other minerals in pure form are harmless, chemically inert, foreign bodies when taken into the lungs. The coarser particles are removed by the ciliated epithelium and swallowed or expectorated. Smaller particles may be phagocytized and removed or deposited in the lymphatics without calling forth any inflammatory reactions. Their ores however contain mixed silicates.

The occurrence of dust diseases in ore workers is probably entirely due to the silica. It is in reality a sidero-silicosis.

Anthracosis.—Carbon particles are, like the minerals in siderosis, chemically inert and produce no pathologic reactions. The former stress laid on the danger of coal dust and miner's phthisis has now given place to the importance of silica contained in the coal.

Chalicosis.—Limestone, marble and gypsum are calcium rocks. The dust particles inhaled during the mining, quarrying, crushing, grinding, cutting, and polishing of these minerals are dissolved in the lungs and removed as soluble carbonates. The lime content itself is harmless. Silica is frequently present in these dusts and is held responsible for pulmonary conditions arising from exposure to them.

Vegetable Dusts (Byssinosis).—Changes produced in the lungs by inhaled vegetable substances is called Byssinosis. The vegetable matter is in the form of fibers which are generally too large to be able to reach the respiratory epithelium.

Cotton, jute, tobacco and wood fibers are the chief offenders. Cotton and jute mills are notorious dust producers. The fibers of these materials, and other dusts contained in them, are thrown into the air during the processes of cording and roving and to a lesser extent in spinning, winding and weaving. Almost all of these dusts are irritating to the upper respiratory tract, and produce chronic naso-pharyngitis and bronchitis.

No demonstrable pathology has been demonstrated in the lung tissue which can be claimed to be due to the vegetable fibers alone. Because of their connective-tissue nature, the silica contained in them may be harmful provided the dust particles are small enough to penetrate the respiratory bronchioles. Sugar-cane fiber contains less than 2 per cent silica.

Tobacco and wood dusts do not produce local pulmonary disease

but may set up allergic responses in the respiratory tract. Sawdust from redwood and teak are the commonest specific irritants of this nature.

Environmental factors in dusty trades are frequently of greater significance to the health of the workers than the dusts themselves. These are, temperature, humidity and air-movement. They are dealt with more fully in the section on Atmospheric Conditions, page 349. In connection with the present discussion, these factors are of great importance in determining the extent to which dusts are suspended in the air and the distance which they travel. In general a hot, moist, still air will hold particles longer and in greater concentration than under opposite conditions. On the other hand, moist conditions on the surface of materials which are being handled will reduce the amount of dust arising from them. Still, dry air will permit small dry particles to remain suspended for long periods and rapidly moving, dry air will waft them rapidly away.

Combinations of these factors must be taken into consideration when studying the possibilities of dust hazards in specific industries.

PROTECTION AGAINST AIR-BORNE PARTICULATE MATTER.

From Cosmopolitan Sources.—Some of the pollenating, allergy-producing plants are common ubiquitous weeds and should be removed for the good of all sensitive subjects living in the community. Such are the ragweeds, goldenrod, pig-weed, lamb's quarter, plantain and some of the grasses.

Other grasses are ornamental and lawn grasses, and control over them is more reasonably attacked on the immediate neighborhood or home basis.

Many shade and nut-bearing trees and ornamental shrubs such as lagustrum are non-essentials and in areas where they are proven to be prolific sources of irritation might reasonably be replaced by inoffensive varieties.

The remainder of the sensitizing proteins are acquired during the daily routines and practices of individuals. Prevention in these instances rests on the knowledge of individual susceptibility. Where it is known that a person is responsive to orris root or corn powder, warning against their use should be sufficient. The same is true in the case of wood workers in teak, redwood and boxwood. One who knows he is sensitive to cotton or kapok should not use pillows or mattresses made of these materials.

House dust cannot be avoided but it can be minimized by frequent airing and cleaning of upholstery and carpets, and by the use of a damp cloth for dusting. The use of oil mops and cloths for floors and furniture is of value. Suction-cleaning apparatus should not be relied upon to prevent dust raising.

Most of the sensitizing animal products come from pets, farm or laboratory animals, or wearing apparel. Unnecessary pets should not be tolerated in a household where any member is sensitive to them, even though a particular animal to which a member is sensitized may not be in the home. *This is due to the fact that animal* sensitization may be a group reaction and not confined to one species.

Because hypersensitiveness does not necessarily result immediately *after contact with a foreign protein but frequently requires* long periods of exposure or some other intervening predisposing factor, and because of its probable constitutional (if not hereditary) nature it would appear to be an intelligent precaution to prohibit *pets in families where there is an antecedent history of allergy of* any kind. The same precaution may be taken against many of the other common sources, such as the use of lagustrum shrubs for ornaments about the house.

Although therapeutic desensitization is a curative procedure its use against recurrent seasonal asthma and hay fever may be considered preventive.

When the source of the allergen cannot be avoided and circumstances *permit, it may be necessary to take up residence in other* parts. Seasonal allergic diseases may be evaded by going away from the neighborhood just before the time of pollenation of the responsible plant. The sea voyage is of value in avoiding these same types of sensitizing agents. Filtered air and otherwise air-conditioned rooms are useful preventive adjuncts for sufferers from air-borne allergens whose living can be adjusted to these limiting conditions.

The protection of the public against smoke and dust nuisances should be taken as a matter of fact by every modern community. While the dusts may not be sufficient to produce serious diseases of the lungs there may be enough irritating materials in them to produce uncomfortable conditions of the upper respiratory tract. Wet street-sweeping and cleaning should be the only method allowable; dust-producing factories should be restricted by nuisance ordinances; all streets should be paved whenever possible.

Industrial Sources.—Dusts in industry arise under controllable conditions and it should be possible to intercept them somewhere between their sources and the tissues on which they act. This intervention must be practical, economic and effective; it will necessarily vary according to the conditions under which the obnoxious agent arises.

Prevention in dusty trades may consist of:

(*a*) Measures taken against the formation of dust at its origin.

(*b*) Measures to prevent dust dissemination.

(*c*) *Measures to prevent the inhalation of dust.*

Under the first are such measures as the substitution of metal abrasives for sandstone in sandblasts, and carborundum for silicate stones in grinding wheels; the use of water or oil in drilling, sawing, grinding, polishing, and blasting; perfection of drilling and cutting tools which are more effective and less dust producing.

Dissemination of dust can be prevented by means of mechanical hoods around the object worked upon and between it and the worker. The sandblast barrel or cabinet is an example. Pneumatic drills may be provided with a hood that surrounds the drill head, and an exhaust that operates through the drill. Humidification of air may be successful under limited circumstances. It is used most effectively in cotton mills where this does not interfere with the manufacturing processes. Electrical precipitation of dusts in exhaust pipes by ionization has proven successful and has been tried with some success at mine heads following blasts. This method has wide applicability and awaits further perfection.

The exhaust system is the most generally applied measure against the dissemination of dust after it has once reached the air of enclosed rooms. In this method exhaust outlets are located at strategic points and the velocity of air through them is controlled. By this means the dustiest atmospheres can be kept down to the accepted standard of 10 to 20 million particles per cubic foot.

Small job processes can have many types of combination hoods and exhausts to meet their particular needs. In such instances as glass etching it is sometimes practical to do this work under water. Larger processes can employ sprays or water curtains between the operation and the remainder of the workroom.

The dust mask is the only practical method of preventing the inhalation of dust. The earliest form and that still most commonly used is a simple filter made of piles of muslin, cheesecloth, or cotton wool. To be effective they must be well made, readily cleaned, adjustable, and comfortable. Workmen prefer to do without masks and will only use them when forced to and then only if they are comfortable. The modern efficiency mask depends upon the creation of a positive pressure within the mask. The clean air is brought to it under pressure through a flexible hose. This type of mask is very efficient but its use is limited to jobs in which the workman is only required to move about in a small radius, generally not more than 10 feet.

No dusty trade can be made dust free and it is not necessary that it be entirely so. The non-silicious dusts can readily be reduced to 20,000,000 to 25,000,000 particles per cubic foot which leaves a sufficient margin to be dealt with effectively by the protective mechanisms of the body. Silicious dusts should be reduced to 10,000,000 or less, if the particles are minute.

Whatever the preventive measures may be the worker must understand the hazards of a dusty atmosphere. Regulations of

employment should consider hours of work and numbers of shifts per day, and in industries where heavy silica dusts are constantly encountered, should take into consideration the days of work per year or even years spent in the trade. Regular medical examination of workers should be accepted as a responsibility by the conscientious employer. Until silicosis is included in the Workmen's Compensation Act, Industrial Physicians and all others concerned are under obligation to point out the dangers of this disease to working men, employers, and legislators. Municipal and State Sanitary Codes in some areas require the use of protective appliances in dusty trades but they do not possess the gravity of Federal Acts and are too frequently ignored or evaded.

CHAPTER XV.

POISONS ACQUIRED BY INGESTION.

Poisons may be taken into the alimentary tract knowingly or unsuspectingly. They may be common beverages or drugs such as alcohol, caffeine, strychnine, and paregoric, or food contaminants like arsenic, lead, fluorine and the toxic products of *Clostridium botulinum*. They are all chemical agents and depend on their chemical state and nature for their toxic effects. Thus the local escharotic effect of carbolic acid on the mucous membrane of the mouth and esophagus is no more nor less chemical than the action of depressant drugs on the central nervous system.

Within the category of ingested poisons are included therefore all substances taken in through the mouth which react chemically with the body tissues and produce harm. These will include ingested drugs, the so-called "common" poisons (accidental, homicidal and suicidal), medicaments and therapeutic agents, poisonous vegetable and animal food substances, chemical adulterants, contaminants and preservatives of foods and beverages, and products formed in the deterioration of foods.

Probably everyone can be said to ingest some one or more poisons every day. That they do not produce more noticeable effects may be due to the small amounts taken or the efficiency of the defense mechanisms of the body against them. Little is known of the possible effects of long-continued exposure to minute quantities of potential poisons and the bearing this may have on the development of some of the unexplained so-called degenerative processes of later life. With one or two exceptions such as the rôle of lead in the etiology of arteriosclerosis, the possibility of such connection is at present in the realm of pure speculation.

The moisture and secretions of the alimentary tract are the first elements in the defense mechanism of the body against ingested poisons. Their first effect is simple dilution.

The effectiveness of the diluent will depend on its relative proportion to the strength and activity of the chemical concerned and on the solubility of the chemical poison in it. On the other hand solution of the poison may be distinctly harmful, as when the acidity or alkalinity of the secretion favors the solution of the poison in an active form and is not sufficient to dilute it to harmless proportions.

Acid or alkaline juices may neutralize some poisons or combine with them to make them inert.

The presence of the foreign chemical may call forth an increase

in the secretions which dilutes it still further and aids in its elimination. The latter is obtained by increased peristalsis of the intestine and evacuation by bowel. When the irritant first affects the esophagus or stomach the vomiting reflex may cause it to be ejected immediately.

Poisons may be rendered harmless before absorption by combining with proteins in the gastro-intestinal tract or by precipitation by the sulphides.

The epithelial lining of the stomach and intestines is a highly efficient filter for all colloidal poisons and many permeable crystalloids are changed or have their toxic properties reduced in passing through the mucous membrane. Lillie[1] points out the possible defensive rôle of the intensively chemically active zone of the close-packed nuclei of the epithelial cells through which poisons must pass during absorption. Histamin is pointed to as a classic example of a powerful toxic agent existing free in the intestinal lumen but prevented from absorption in toxic amounts by the normal epithelium.

After absorption the defenses so far as known are simple chemical processes of oxidation, reduction, hydration, dehydration, and addition. Wells[2] summarizes the resistance to chemical poisons by stating that "the neutralizing substances do not appear to be the result of any special adaptation to meet a pathologic condition. They are present in the body as a result of normal metabolism; they have an affinity for various chemical substances, some of which happen to be poisons; if these poisons happen to enter the body they may be combined and neutralized to some extent, but, as a rule, very incompletely."

Intoxication results when the normal defenses are inadequate because the strength or amount of the poison is overwhelming, or because the protecting substances have been diminished through physiologic or pathologic changes, or there is pre-existing pathology that is favorable to absorption.

Since the prevention of these poisonings depends upon the institution of measures to prohibit their being taken in harmful quantities it is necessary to consider the manner and circumstances in which they are acquired. For this purpose they have been classified under the joint consideration of where they exist in the environment and the conditions under which they are consumed.

1. Taken as food or beverages.
2. Taken with food or beverages.
    (a) Food adulterants and preservatives.
    (b) Food contaminants.
    (c) Decomposed food products.

[1] Lillie, R. S.: Am Jour. Physiol, 7, 412, 1902

[2] Wells, Gideon: Chemical Pathology, 5th ed., Philadelphia, W. B Saunders Company, 1925.

3. Taken or given as medicines.
4. Taken as drugs (addiction).
5. Taken by mistake or carelessness.
6. Taken or given as suicidal or homicidal poisons.
7. Acquired from industrial sources.

POISONS TAKEN AS FOOD OR BEVERAGES.

Poisonous Mushrooms.—There are three important poisonous mushrooms—*Amanita muscaria*, *Helvella esculentia*, and *Amanita phalloides* (the Death Angel). Their active toxic principles are respectively, muscarin, helvellic acid, and amanita-toxin. The first two are members of the "saponin substances" group of glucosides. Amanita-toxin is neither a glucoside nor a protein. Muscarin and helvellic acid are destroyed by heat but amanita-toxin is thermostable. (*Amanita phalloides* also contains a relatively less important toxic glucoside, phallin, which is destroyed by heat and digestive juices.)

Muscarin is a nerve poison and acts by stimulation of the peripheral motor and secretory receptors (atropine depresses the same receptors). In poisoning from *Amanita muscaria* therefore there is excessive stimulation of secretions, and increased smooth muscle activity. These are revealed by salivation, diaphoresis, watery diarrhea, vomiting, retching, abdominal cramps and violent peristalsis.

Amanita-toxin from *A. phalloides* is a protoplasmic poison which produces widespread fatty degeneration of parenchymatous organs. Phallin, from the same species is a hemolytic phytotoxin. Poisoning from *A. phalloides* is slow and delayed, due to the results of the cellular degeneration. Phallin does not ordinarily produce symptoms because it is destroyed by the digestive juices. Death occurs from suppression of the urine and damage to the liver.

Solanin.—Solanin poisoning results from the ingestion of a powerful hemolytic and protoplasmic poisonous saponin called solanin which is found in all parts of young sprouting potatoes. This is a rare occurrence because sprouting potatoes are seldom eaten as such and the ordinary new and old potatoes do not contain the poison.

The hemolytic effect of solanin taken by mouth is slight if manifested at all. The principal effect is on the nervous system and parenchymatous organs. Large doses paralyze the heart and central nervous system centers. It produces gastro-intestinal irritation with vomiting and collapse and its degenerative effect on the liver causes jaundice, chills, fever and prostration.

Ergot.—*Claviceps purpurea* is a poisonous fungus which grows on rye and occasionally other grains. It contains two active alkaloids, ergotoxin and ergotamin and two pressor substances, tyramin and

histamin. These all have an epinephrin-like effect and in addition the first two have an action on the medullary centers.

The typical smooth-muscle action of these substances results from their stimulation of the motor myoneural junctions. Prolonged intoxication results in chronic arteriolar contraction with ischemic gangrene of the parts supplied. Most commonly, gangrene is seen in the extremities but it may occur in internal organs as well.

Poisoning from ergot results from the ingestion of cereals and breadstuffs made from infected grain, generally rye. The amount consumed in a single case and the detoxifying efficiency of the intestinal mucosa practically preclude the possibilities of acute poisoning. Cases have occurred however and are generally ascribed to absorption through previous lesions beyond the portal drainage area.

Ergotism is rare in the Western Hemisphere and is seen less frequently in the European Continent than formerly when it used to assume epidemic proportions. It is probable that many of the reported effects of ergotism in these widespread attacks were complicated by other conditions such as meningitis or avitaminoses.

Lathyrism.—*Lathyrus sativus* and *L. cicera*, (chick-pea or vetch) contain a powerful neurotoxic agent which has not been certainly identified. There is evidence that it may belong to the group of phytotoxins along with ricin and abrin, but Stockman[1] considers it with the alkaloids.

If it is a phytotoxin it is probably a part of the protein molecule and exists as a toxalbumose. The phytotoxins act like bacterial toxins in possessing haptophore and toxophore groups and having the power to produce immune substances against them. If it is an alkaloid these properties will be lacking.

Vetch is consumed in India as a cereal substitute for wheat in making meals and bread. It is used occasionally in Europe and parts of Africa.

The neurotoxin appears to be selective for the upper motor neuron of the cord as its action results in spastic paralysis of the lower extremities, lumbar pains and girdle sensations. Complete spastic paraplegia may result: occasionally the upper extremities may be similarly affected.

Bitter Almond.—The bitter almond, *Amygdala amara*, is the ripe seed of *Prunus amygdalus* var. *amara*, indigenous to Asia and cultivated in Spain and the Balearic Islands. It contains a glucoside, amygdalin and an emulsin, which together in the presence of water produce hydrocyanic acid through a process of decomposition.

The ingestion of as few as three bitter almonds by a child has resulted in fatal poisoning. Almond paste made from ground bitter almonds may also be a source of this poison. The effects are those of hydrocyanic acid and are discussed elsewhere under this poison.

[1] Stockman, R.: Edin. Med. Jour., 19, 277, 1917.

Oil of bitter almonds contains from 2 to 4 per cent of prussic acid. Seventeen drops have proved fatal to a man.

Fish Poisons.—Aside from the poisonous substances on the defensive spines of some fish and the decomposition products that develop in killed fish there are certain toxic bodies present in a few varieties of fish even when perfectly fresh.

The important poisonous fish are:

Tetrodon—(Fugu) The parrot fish of Japan.
Barbus fluviatilis—The barbel.
Esox lucuis—The pike.
Acipenser sturio—The sturgeon.
Lepidosteus sp.—American gar.

In each of these the poison is confined to the eggs (roe) and ovaries. Tetradon-toxin appears to be non-protein (a gluco-ester according to Ishiwara[1]) while the toxins of the others are associated with the protein molecule. None possess antigenic properties.

Tetradon-toxin or fugu-toxin (Ishiwara) is anesthetic to motor nerve endings, and paralytic to motor and sensory nerves, but does not affect the sympathetics. Local gastro-intestinal symptoms range from those of a "ptomaine poisoning"—like attack to the rapidly fatal algid reactions as seen in cholera.

The toxins of the other roes act as respiratory paralyzants.

Tahara determined the minimum lethal dose of fugu-toxin as 0.0025 to 0.004 gram per kilo.

Poisoning from all of these fish results only when the roe or ovaries are included in the ingested portions. Thus, only one or more of a party may be poisoned from a single fish unless all partake of the roe.

Vomiting and diarrhea may eliminate enough of the toxin to prevent serious poisoning.

Mussel Poison.—The edible mussel, *Mytilus edulis* (England, Europe), *Mytilus californianus* (Pacific Coast of the United States) contains a poisonous amin which appears to be related to the spawning season because cases of poisoning suspected of being due to it occur only between the months of May and October. This form of poisoning according to Meyer[2] is not due to mytilotoxin, which is a ptomain, originally described by Brieger in his classical investigation of the Wilhelmshauser cases in 1885. The term mytilotoxismus should be applied only to poisoning by mytilotoxin and not to mussel poisoning due to the specific seasonal amin. Probably many cases of mussel poisoning are due to mytilotoxin and must be looked upon as ptomain poisoning from the ingestion of decomposed mussels.

The mussel amin resembles fugu-toxin chemically and pharma-

[1] Ishiwara, F: Arch Exp. Path. Pharm, 103, 209, 1924.
[2] Meyer, K F *et al*: Jour. Prevent. Med., 2, 365, 1928.

cologically. It is thermostabile and therefore not destroyed by cooking. Sodium bicarbonate in the proportion of ¼ ounce per quart of boiling water will destroy the poison in twenty to thirty minutes.[1]

Food Allergens (Anaphylactogens).—The chemical agents in food which are responsible for the phenomena of food allergy are the proteins. These, in the belief of Wells are only the whole proteins. There is some evidence that polypeptids may be responsible at times so that this point cannot definitely be closed.

The mechanisms of allergy are discussed further in the sections on Poisons Acquired by Inhalation (page 181) and Invading Organisms (page 485). It is only necessary to state here that proteins introduced by way of the gastro-intestinal tract initiate and take part in processes of allergic reactions in the same way as those which enter through respiratory epithelium.

Although much is known on the experimental and theoretical sides of allergy there remain wide gaps in the interpretation of clinical experiences with suspected food allergies. The known mechanisms of sensitization form but part of the natural history of allergic diseases. Between the proteins as they exist in natural foods and their earliest participation in allergic phenomena lies a zone of almost complete ignorance as to how they are enabled to become agents of disease. Under healthful conditions food proteins exist only as potential allergens and are no more harmful than the other food elements. Under some unknown circumsfances they assume harmful qualities. Hypotheses point to some co-existing defect in the absorbing mechanisms which permit large protein molecules to enter the body tissues or to some constitutional factor or inheritance, which prepares the way for absorbed proteins to initiate reactive processes against them. It is difficult to prove absolute relationship between allergic phenomena and any given proteins in the diet even in the face of positive sensitization tests to the proteins, and there are many instances of allergy with negative tests on all available forms of protein. The latter predicament may be due to inadequate investigation or ignorance of all possible proteins.

From this it is obvious that food proteins are the *sine qua non* of food allergy and not the sole cause, and the search must continue for the agent responsible for the circumstances under which ingested proteins become actual anaphylactogens.

The common food proteins responsible for allergic conditions are found in milk, eggs, nuts, meats, wheat, fish, radishes, coffee, barley, and some fruits.

There is no uniformity in the clinical types of allergy which may result from sensitization to the proteins of these foods. Some patients show asthma, others eczema and still others acute edema of

[1] Muller, H.: Weekly Bull. Calif. State Dept. Health, 11, 138, 1932

various tissues. Even in the same patient the phenomena may differ from time to time from eating the same food on each occasion. This has been called the "substitution phenomenon."

Edema is the common factor in most of the allergic phenomena. It is due in part to vasomotor disturbance, change in capillary permeability and alterations in osmotic pressure. An attempt has been made (Wells) to place anaphylotoxin in the position of the common causative agent of all anaphylactic reactions but this is not entirely accepted.

Depending on factors such as area and tissues involved, temperature and exposure of parts, acuteness or chronicity of the condition, age, sex, and inheritance (possibly) the lesions will assume one or more of many varieties. The commonest clinical evidences of sensitization to ingested proteins are urticaria, angioneurotic edema (skin or visceral), eczema, erythema multiforme, vasomotor rhinitis, conjunctivitis, asthma and possibly migraine.

Alcohol.—Ethyl alcohol (CH_3CH_2OH) is a chemical poison. This statement is not minimized by the fact that it is a readily available source of energy, a protein saver, and a substitute for the energy producers—carbohydrates and fats. It is completely oxidized in the body and eliminated; none of it can be stored in the tissues to be drawn upon later. Whatever claims can be held for ethyl alcohol as a food are limited to the above experimentally demonstrated facts which remove it from the category of tissue-building foods and leave it as an energy producer and tissue-conserver. Ethyl alcohol is primarily a central nervous system narcotic. It is a cerebral anesthetic which early involves the higher powers of judgment and discrimination and thus alters behavior. Agreement is almost general that alcohol is a cerebral depressant and does not stimulate the brain; what is ordinarily spoken of as stimulation is more likely a reduced activity of the intellectual and emotional controlling mechanisms, and the release of unbridled reactions to simple situations.

Alcohol is absorbed directly through the mucous membrane of the stomach and intestine without the necessity of undergoing digestion. It is absorbed more quickly on an empty stomach and its absorption is delayed longer when fats are present. Milk is the food which retards it longest.

Within the stomach, alcohol is detrimental to the action of ferments but accelerates secretion. It also lessens stomach contraction if taken in more than moderate amounts. Excessive quantities are gastric irritants and bring about catarrhal changes when used over long periods. Mucus is secreted in large amounts following excesses of alcohol.

The influence of alcoholic beverages on appetite and digestion

is a complex of psychologic and physiologic reactions to the situation and circumstances under which it is consumed; the like or dislike of the consumer for the type of beverage; the stage of digestive activity at the time; the strength of the drink; the aromatic and other qualities, favorable or unfavorable, which it may possess; the rapidity with which it is drunk and individual tolerance to it. The latter appears to be an increased ability to oxidize alcohol in the tissues. Furthermore, the habitual drinker shows less reaction in the brain than the occasional drinker or neophyte.

During even mild intoxication alcohol slows down reflex activity and reduces the efficiency of finely coördinated movements. These effects coupled with reduced judgment and discrimination manifest themselves in the inability to perform acts of skill and in an increased tendency to accident.

The effect of alcohol on respiration and circulation is inconsequential except in extreme narcosis. Death from pure alcoholism is due to respiratory failure.

Pure ethyl alcohol consumed in moderate amounts and temperately has not been proven to produce any permanent harm. The former conception that alcohol was the only cause of cirrhosis of the liver can no longer be sustained. Considerable doubt is thrown on the idea that alcohol alone can produce arteriosclerotic or other degenerative changes in the body. It can however bring about overweight and obesity when taken over long periods along with an adequate fat-producing diet. Fatty infiltration, degeneration of blood-vessels, heart and liver may accompany the general adiposis.

Excessive, prolonged use of alcoholic drinks leads to a chronic progressive state characterized largely by nervous and gastro-intestinal changes. Alcoholic neuritis with tremors is a common sequel to overindulgence, but there is evidence that this may be due to a defective vitamin intake. In the central nervous system, meningeal irritation results in increased secretion into the ventricles and meningeal thickening. Accompanying this there may be mental deterioration and a delusional insanity. Korsakow's syndrome is the combination of pathologic lying, peripheral polyneuritis and diarrhea. The gastro-intestinal changes may involve the whole length of the alimentary tract from catarrhal stomatitis and pharyngitis to colitis.

The source of alcoholic beverages is from the fermentation of sugars by the action of a zymase and co-ferment present in a yeast organism, *Saccharomyces cerevisiæ*. The yeast is made to act directly on the sugars or, in the case of malt liquors, the malt starch is first reduced to sugars and the yeast added.

Fermentation alone cannot create an alcohol concentration higher than 14 per cent as at this point the alcohol inhibits the yeast and

prevents further fermentation. Alcoholic drinks containing more than 14 per cent alcohol are obtained by further distillation and concentration or by fortifying them with alcohol from other sources.

The following are the ranges of alcohol content of the common classes of alcoholic drinks:

Beer	1 to 5 per cent
Ales and porters . . .	4 to 9 per cent
French and German light wines	6 to 10 per cent
Clarets, sherry and ports .	15 to 20 per cent
Whiskies and brandies . .	47 to 54 per cent
Rum and gin	50 per cent
Liqueurs and cordials . . .	30 to 57 per cent (absinthe)

In the fermentation of sugar, propyl, amyl, and butyl alcohols, aldehydes and esters are also formed, which considered together are called fusel oil. In prepared liquors they constitute about 0.2 per cent. Although these alcohols are decidedly more toxic than ethyl alcohol their quantity in properly aged drinks is below any harmful amounts.

In addition to the legitimate alcoholic beverages there have been in the past and still are, a number of proprietary preparations with alleged medicinal value and containing relatively high percentages of alcohol. Addictions to their use are many because they afford an easy way to obtain considerable amounts of alcohol under the guise of "taking a tonic."

Coffee and Tea.—As pointed out by Cushny it is odd that so many peoples throughout the world resort to beverages made by infusion from caffeine-bearing vegetable substances when the caffeine content does not reveal itself by any conspicuous characteristics in the plant or by any definite drug effects which the users would be likely to ascribe to it. Through whatever means they came into use, whether accidentally in the search for medicinal herbs or magic potions, or by deliberately seeking for pleasant drinks, they were found to be harmless and remained as pure beverages.

The common caffeine-bearing plants in use today are *Caffea arabica*, the beans of which are the source of common coffee; *Thea chinensis*, the familiar tea-leaf; *Paullinia sorbilis* seeds, from which the Brazilians make Guarana paste; *Ilex paraguayensis* leaves which are infused by the Paraguayans to make Yerba Mate or Paraguay tea; the leaves of the Virginia and Carolina Ilex; and the Kola Nut from *Sterculia acuminata* used by the natives of Central Africa.

Caffeine in some way increases the receptivity of nerve tissue to stimuli. This is evidenced by increased accuracy of the sense of

touch, and in the higher functions by a more rapid flow of thought and association of ideas. Subjectively these reveal themselves as irritability to mild stimuli, keen awareness of surroundings even to the point of hypersensitivity, wakefulness, increased mental and physical output and a sense of greater endurance against fatigue.

The mechanisms through which this wide range of results is brought about remain unknown. That the caffeine molecule in some way enhances nerve reception and nerve-cell conductivity is probable but unproven. Empirically, the user of caffeine gets a nervous "kick" or boost from it although he may not consciously connect his behavior with the beverage. In individuals who appear to be more susceptible to it the results are interpreted as nervousness, insomnia and conscious irritability. This may be translated into physical phenomena such as a generalized trembling of the body, tremor of the hands, and consciousness of somatic sensations such as palpitation of the heart, respiratory deepening and gastro-intestinal hypermotility.

One undoubted pharmacologic effect of caffeine is diuresis. The present explanation of the increase in both fluid and solid contents of the urine lies between the theories of Cushny and Richards. The former presents the opinion that caffeine increases the permeability of the glomerular epithelium while the latter presents evidence that its action is due to an increase in the area of functioning epithelium of the total renal capillary bed.

The consumer of an average cup of coffee or tea takes between 1.5 and 3 grains of caffeine. Caffeine and its therapeutic preparations are administered medicinally in the dose of 2.5 to 5 grains. Even the moderate coffee drinker who takes from 3 to 7 cups per day is therefore consuming 2 to 6 times as much caffeine as a single medicinal dose. Because caffeine directly or indirectly results in a greater output of work (although this may not lead to fatigue as rapidly as under ordinary conditions), it causes a greater expenditure of energy. Custom seems to have recognized this and compensated for the loss by taking sweets (carbohydrates) along with it. The English custom of afternoon tea may be a direct means of stimulating activity toward the end of a working day, and the sweet biscuits and jams are conceivable adjuncts unconsciously taken to anticipate the need for rapidly available energy.

The coffee and tea drinker is taking more than a stained solution of caffeine in water. It contains tannic acid in varying quantities, the amount determining the "darkness" or "greenness," especially of tea. Tea contains 7 per cent tannic acid in the leaves. Of the many volatile substances which give the aroma and bouquet to these beverages furfur alcohol is probably the only one with any

important physiologic effect. This alcohol acts on the gastro-intestinal canal as a carminative and Cushny suggests that some of the pleasant effects of coffee and tea drinking are due to it.

Caffeine is 1–3–7 trimethyl—2–6 dioxypurine or trimethylzanthine; one of the purin derivatives. It is absorbed directly through the gastro-intestinal mucous membrane and carried to the liver. Habituation to its use may depend on refractoriness of the tissues, from the intestinal mucous membrane cells to the cells of the nervous tissues, or to an increased ability of the liver cells to demethylate it and form monethylzanthin, zanthin and eventually urea. A single dose of caffeine is entirely reduced and eliminated in twenty-four hours.

CHAPTER XVI.

POISONS ACQUIRED BY INGESTION (CONTINUED).

PREVENTION OF POISONING BY FOODS AND BEVERAGES.

Non-edible Foods.—Without foreknowledge it cannot be known that the solid foods possessing poisonous qualities are dangerous to health. They do not reveal their toxicity by any warning through obnoxious taste or smell and may on the contrary appear succulent and desirable. This latter is especially true of some of the fish roes and mushrooms.

Fortunately, experience and food customs present the greatest barrier against the widespread use of most poisonous foods and they are obtained only occasionally under special circumstances. The use of chick-pea or vetch for example as a substitute for wheat flour in times of food shortage opens the way for lathyrism to appear in a community in epidemic proportions. Any medical authority in a country where this substitute is resorted to should understand its dangerous nature and issue warnings against it; the occurrence of a single case of ergotism is a danger signal to a populace using rye products and its appearance requires immediate investigation to reveal the source of the infected grain.

Solanin poisoning has occurred among people who consumed premature potatoes prepared as salads for picnics. The potatoes must be young and sprouting for the solanin to be present in amounts sufficient to produce poisoning. The simple precaution of using only matured (new or old) potatoes will prevent this condition. Most instances of sickness after eating potato salads are not due to the solanin content but to infection of the salad medium with pathogenic organisms.

Mushroom poisoning continues to be a serious health menace in spite of efforts designed to inform amateur collectors of the differences between edible and non-edible species. There are over 40,000 species of mushrooms! The most that the amateur can hope to do is to learn the identification of the more common edible forms and leave all others alone. The generic and specific characteristics are not difficult to recognize once one has investigated the morphology of mushrooms generally and learned the names of the parts mentioned in reference works on the subject.

None of the household tests for poisonous mushrooms are of any value *whatsoever and they must not be relied upon no matter how* authoritative the source of information may appear to be.

The alkaloid of *Amanita muscaria* can be rendered harmless by soaking the mushroom in water to which a little vinegar has been added before cooking.

Since the poisonous fish products are confined to the roes of a few species it should be sufficient to instruct those living in areas where these fish appear on the market never to eat the eggs or ovaries.

The health authorities in California prohibit the sale of edible mussels between June and September since this period embraces the time when they acquire their poisonous qualities. Individual collectors may still be in danger of poisoning. It may be avoided by cooking the shell-fish for thirty minutes in water to which sodium bicarbonate has been added in the proportion of one-quarter ounce of soda to 1 quart of water.

Alcohol.—From what is known at present of the physiologic and possible harmful effects of ethyl alcohol on man, the problem of prevention resolves itself into control of its abuse.

There is no scientific support for the necessity for total abstinence in the healthy but there is abundant evidence in favor of the temperate over the excessive use of alcoholic beverages by the individual and society.

Alcoholic intoxication is a world-wide problem and a generally recognized one in every community. Social custom influences in part the amounts and degrees of intoxication so that in one community there may be almost complete voluntary prohibition and in another the most open acceptance of alcoholic excesses.

Medical science can point to no immediate or remote harm from the single acute mild intoxication from high grade alcoholic beverages; it is far less certain of the harmlessness of repeated intoxications over a long period of time; it is positive of the harmful effects of prolonged heavy drinking.

The medical adviser is in a quandary when he attempts to assay the potential harm that may come to a given individual who comes to him asking for information about his specific drinking problem. He knows that scientifically he can go no further than recommend temperance and that if he begins to take the many social aspects of the problem into consideration he is leaving his laboratory. Mental hygiene appears to be the best way out of his dilemma.

No physician can deny the importance of the mental aspects of his patients. He is daily required to aid in mental readjustments of all kinds and every drinker—as well as non-drinker—has his own mental attitude toward alcohol. Alcohol is primarily a mental intoxication and as such should be looked upon by the doctor as being as much a poison to the central nervous system as strychnine. The temporary nature of its effects is the great alibi of the drinker and the doctor who condones its abuse. What every physician

should actually interest himself in in the drinker coming for advice is "Why does he drink?" "Why does he use as little or as much as he does?" "Why is he asking my advice?" In his answer to these lies the only sound basis for judgment on the case before him.

Moral, religious and social attitudes toward drink resolve themselves into standards of right and wrong. The physician has nothing to do with these except insofar as they may lead to physical or mental ill-health.

The aim of prevention must be to lay obstacles in the path of individuals who exhibit evidence that they may be potential chronic alcoholics. If prevention is delayed until the appearance of chronic gastritis, alcoholic neuritis or any other organic effects of alcoholism the story has been entered long after the onset of chronic alcoholism. Interference at this stage is cure, not prevention. It is this inability to prophesy that makes the problem of prevention so difficult. The best expediency at present may be for the physician to adopt the principle of probability whenever he is approached on the subject and recommend reduction of intake and treat the patient on psychologic grounds

The influence of alcohol on the progress of associated organic diseases such as diabetes, gastric ulcer, or arteriosclerosis is more clearly defined. The strictly medical aspects of these conditions warrant unreserved control of alcoholism in their presence.

In summary, the conscientious and intellectually honest physician cannot do other than teach alcoholic temperance. He knows the dangers inherent in lack of control and is convinced that abuse is not without possible serious consequences. To excuse himself on the basis that he is exempt from giving moral judgments is evasion of his medical duty.

Caffeine.—It is common to find coffee drinkers who blame every uncomfortable feeling they may have on coffee; more frequently there are found those who connect only sleeplessness or difficulty of going to sleep with this beverage; there are some who claim that *coffee does not affect them in any way.*

That there is a psychic element in the alleged effects of coffee can hardly be denied. Although it may be admitted that caffeine augments cerebration it is highly probable that anticipation of its effects may lead to marked exaggeration of its action. The person who holds tenaciously to the idea that coffee keeps him awake will undoubtedly be kept awake by small and otherwise ineffectual amounts. The habitue on the other hand may fall asleep readily after drinking a late black cup.

Aside from tremulousness, this inability to go to sleep is the only effect of coffee which is commonly attributed to it. Although intolerance to caffeine may be present it is more often apparent than real and the *sleeplessness is compounded of many elements other than*

caffeine. Granting that this be but partly true, prevention of its so-called poisoning is a matter of training if the habit is to be continued. Otherwise abstinence from the evening cup is the concession that must be made by the apprehensive drinker.

Idiosyncrasy to the drug may exist in some but it is hard to prove. When it is highly suspected and regulation has failed to reduce its effects, abstinence alone will bring about relief.

There is a strong tendency among certain classes to allow children to drink coffee. This is inexcusable because children develop habits of eating very readily and in this instance develop a preference for coffee over more nourishing foods. In them there is also a greater opportunity for caffeine to exert its true effects at night by stimulating them excessively just before going to bed.

Undesirable remote effects of coffee are tremors, cardiac palpitation and gastric irritation, the latter from ingredients other than caffeine. When any of these are present reduction in the daily amount of coffee is indicated. Too little is known of the remote effects of the continued use of caffeine after its definite toxicity has been revealed, to permit a casual attitude toward it. Caffeine is a real tissue poison and should be respected as such.

CHAPTER XVII.

POISONS ACQUIRED BY INGESTION (CONTINUED).

POISONS TAKEN WITH FOOD OR BEVERAGES.

(*a*) **Food Adulterants and Preservatives.**—Prior to the passage of the United States Pure Food and Drugs Act in 1906 there was much discussion on the harmfulness of various chemical substances which were added to foods for one purpose or another. This practice had been branded as adulteration in 1895. Although the number of chemicals employed was small they were all recognized and classed as poisons. The proponents of the Pure Food and Drugs Act were strongly convinced that these alleged poisons were detrimental to health and their use was condemned. To support their contention they employed what has now become the historical "Argument of Small Quantities." By means of a double graph showing an inverse proportion between the harmful effects of a poison starting at zero dosage and rising as it approaches its lethal dose at 100 and the curve of a diminishing food intake which starts at 100, its normal (the amount of that food which maintains a healthy adult body in equilibrium) and rises as it approaches its "Lethal Dose," zero, Wiley[1] attempted to show the fallacy in the argument that small quantities of a substance are not injurious. Wiley concludes with the statement, "It is easy to show by mathematical data that no matter how small the quantity of an injurious substance or preservative it will still produce an injurious effect which may be infinitely small if the dose be infinitely small. It follows then, as a mathematical demonstration that any quantity of an injurious substance added to a food product must of necessity be injurious provided it is in the nature of a drug and the body is in a perfectly healthy normal condition. Hence the argument which has been so persistently urged in favor of a chemical preservative, that if in small quantities it is harmless, is shown to be wholly untenable."

Those who argued in favor of the harmfulness of small quantities evidently believed in "once a poison always a poison" and took no account of the possibility that small doses might exhibit no poisonous qualities whatsoever.

Chemical adulterants "may" be poisonous when taken in certain amounts and possibly over certain periods of time. As a result

[1] Wiley, H. W.: Foods and Their Adulterations, Philadelphia, P. Blakiston' Son & Co., 1907.

opinion has changed considerably over the possible harm of some of the present-day adulterants as now used.

Estimates of the amount of food adulteration in the United States and England before 1906 range from 50 to 80 per cent of the commercial food products. This however was not all due to the use of chemical adulterants and preservatives which are the only forms of adulteration (as legally defined) now under consideration.

The common chemicals added to foods for preservation of their taste, color and edible qualities, or as deliberate fraudulent additions were, and still are sodium borate and boric acid, sodium nitrate and sulphite, acetic acid, salicylic acid, formaldehyde, copper sulphate, saccharin, anilin and coal-tar dyes, iron oxide, iron sulphite, arsenic, lead, hydrofluoric acid, sodium fluoride, and vegetable dyes.

Some of these are permitted and condoned by medical authorities on the basis of the small amounts used but the Department of Agriculture which administers the Food and Drugs Act in America is less lenient in the interpretation of its law, basing its decisions more on economic than medical grounds.

Arsenic, salicylic acid and lead are generally condemned on all sides. There is little evidence against the remainder in the amounts used on the argument of proven toxic effects. However, suspicion is strong enough against some to condemn them. Anilin[1] has recently been suspicioned as being the cause of an allergic dermatitis; saccharin is alleged to produce vague gastro-intestinal indigestion following its prolonged use; formaldehyde is believed to interfere with the proper digestion of proteins and starches; fluorides have been proven to produce "mottled enamel" in children.

The indirect effects of adulterants and preservatives in lowering the quality and grade of foods and the harm which is brought about by fraudulent deception of the consuming public are factors beyond the scope of the category of chemical toxic agents.

(*b*) **Food Contaminants.**—Food from various sources and processes of preparation and marketing may become contaminated with harmful chemicals.

Arsenic.—One of the most interesting forms of poisoning associated with the taking of food is its contamination with arsenic. The classical example was the epidemic of neuritis which occurred at Manchester, England in 1900. In this instance iron pyrites containing arsenic as an impurity was used in the manufacture of sulphuric acid and the acid, in turn, was used in making glucose. The arsenic was carried over with the glucose which was used to make a cheap beer, and thus some thousand cases of arsenical neuritis occurred from drinking this contaminated beverage. Rosenau records that the beer contained from 1 to 3 grains of arsenic per

[1] Baer, H L.. Jour. Am. Med. Assn. 103, 10, 1034

gallon. Similar poisoning can occur through the use of contaminated glucose used for any other food purposes.

As late as 1912, Bernard Smith[1] of the Boston Food and Drug Inspection Laboratory found harmful amounts of arsenic in commercial shellac used for glazing the surface of cheap candies and confections. Smith states that "Orpiment (yellow sulphide of arsenic) is very generally added to shellac in India for the purpose of rendering the product opaque and producing the light-straw color of the higher grades." Shellac of this type was formerly widely used in lining tins, vats, and containers, especially those for brewers' products.

The use of arsenical sprays to control insect pests in orchards and gardens has raised the question of an arsenic hazard to the consumers of such treated fruits and vegetables.

The two commonest arsenical sprays are arsenate of lime and arsenate of lead mixtures. Arsenate of lime mixture contains 1 pound of white arsenic per gallon of fluid and arsenate of lead mixture 4 ounces of arsenate of soda, 11 ounces of acetate of lead (sugar of lead) to 100 gallons of water. Paris green (a double salt of copper acetate and meta-arsenite) and Scheel's green (copper arsenite) are also used as sprays in the proportion of 1 pound of either to 150 gallons of water. The coating of the arsenical suspension on the fruits and vegetables can readily be removed for the most part by washing and rinsing with water. Acidulated water appears to be more effective. All of the arsenic cannot be removed because part of it undergoes combination with the plant tissue itself.

Small amounts of arsenic on sprayed fruits and vegetables are not considered injurious to health and the U. S. Food and Drugs Act administrators place the allowed maximum at 0.01 grains of arsenic (as AS_2O_3) per pound of food. This is in the proportion of 1.4 parts per 1,000,000. Coulson[2] has shown in a preliminary contribution that organically combined arsenic in shrimp is stored far less effectively in the bodies of experimental rats than inorganic arsenic trioxide administered in the same dose as the amount of the naturally occurring compound in this sea food.

Arsenic poisoning is due to the arsenious acid ion. Dissociation of this ion from the organic compounds is difficult and this fact probably explains their relatively low toxicity. The anhydride and organic salts on the other hand are readily converted to arsenious acid and in the tissues probably form arsenites. Arsenical salts and acids do not possess the typical garlicky smell of volatilized arsenic and are therefore not detectable by their odor. They do not possess any characteristic taste which will reveal their presence in food. The sweet taste attributed to them is too mild to be noticeable.

[1] Smith, Bernard Circular 91, U. S. Dept. Agric., Bur. of Chem., 1912.
[2] Coulson, E. J. *et. al*: Science, 80, 230, 1934.

Arsenic in small doses acts as a protoplasmic poison to the epithelial cells lining the stomach and intestine and to a less degree in other viscera. The observed effect is a fatty infiltration of the cells. Between this and an accompanying vaso-dilatation and congestion, lies the explanation of the superficial similarity in the appearance of the stomach and intestine in arsenic poisoning and the action of the true corrosives. In the case of arsenic, the membrane is damaged by a true protoplasmic change which interferes with function; the corrosives destroy the cells completely.

The direct action of arsenic on the capillary walls results in their dilatation and increased permeability to fluids. Extracapillary accumulation of fluid takes place producing edema and serous exudation. This explains in part, the watery stools of acute arsenical poisoning.

In the chronic form of poisoning nitrogenous substances appear in the urine in increased amount and the liver loses a great part of its glycogenic function. Fatty degeneration, much resembling that due to phosphorus, occurs in the parenchymal cells of the liver, blood-vessels and lungs and the muscle cells of the heart. Some of the metabolic effect is attributed to an acceleration of autolysis.

There is a strong tendency for the body to store up arsenic which has been absorbed but there is always some immediate loss by way of the urine and feces. That which has been retained is held by the cells of the viscera for some time but has a strong predilection for epithelial tissues. Thus it is found in considerable quantities in the skin and hair. Since the epidermis and hair are eventually shed, arsenic is gradually lost in this way. In chronic poisoning it is likely that there is a continual shift of stored arsenic from tissue to tissue.

Lead.—Lead gains access to foods and beverages through gross contamination as they are being eaten and by previous contact with the metal or its salts at its source or in transport.

In the first category fall such instances as the contamination by lead on the hands of workers who handle lead products. Painters and other lead workers who are careless about washing their hands before meals may carry poisonous quantities of lead to their mouths while eating; workers who eat their lunches in a lead-laden atmosphere may consume gross amounts of the metal which has settled on their food.

The second category contains such sources as soluble lead salts or even the metal itself which comes from lead pipes or cisterns, or pipes sealed with lead solder; beverages prepared in lead sealed vats or stills; small food containers such as tin-cans and tinfoil in which lead is used; lead-containing sprays for pest control on fruits and garden products.

Rosenau cites two instances of multiple poisoning caused by

drinking lead-contaminated water, one in a convent near Lyons and the other at Château de Claremont. In the first the contamination amounted to 2.7 mg. of lead per liter and in the second 16.5 mg. per liter.

The lead solvent power of all water is not the same. The conditions which favor and suppress the passage of lead ions into water may be listed as follows:

Favoring contamination:

Carbonated water or water with a high CO_2 content.
Water with a pH value below 7 and above 9.5.
Pure water—distilled water especially.
Soft water.

Suppressing contamination:

Deposits of lead oxide or carbonate inside the container.
Turbid water.
Water with a pH value between 7 and 9.5.

The lead spray for pest control contains 11 ounces of acetate of lead (with arsenic in the same proportion) per 100 gallons of water. Some of this may remain in the inaccessible crevasses of fruits, vegetables and leafy plants even after the most thorough washing. The U. S. Food and Drugs Act prohibits the sale of foods containing more than 0.014 grains of lead per pound or 2 parts of lead per 1,000,000. The allowable limit recommendeed by the Advisory Committee on Standards for Drinking Water of the U. S. Public Health Service is 0.1 parts per 1,000,000.

Lead chromate has been used in bakers' supplies to give color to cakes and confections and has produced poisoning.

Ingested lead is not readily absorbed because of the high tendency for the formation of insoluble sulphur compounds in the intestinal tract. Even that which is absorbed may be eliminated largely through the bile. Although poisoning by ingestion is now less common and far less hazardous than inhalation of lead dusts it is still an actual potentiality of serious grade under the conditions mentioned. The form in which it is taken, the circumstances under which it is acquired, and the conditions in the defense mechanisms of the individual all go to make it quite impossible to set any minimal toxic dose. It is said that 0.5 mg. of lead per liter or $\frac{1}{33}$ grain per gallon of water may produce poisoning if taken continuously.

For a continued discussion of the mechanisms of lead poisoning after absorption has taken place, the reader is referred to the article on lead acquired by inhalation.

Copper.—Copper poisoning resulting from its ingestion in food is rare and by some is not conceded to occur at all. Animal experimentation however, has demonstrated that copper in small amounts can be absorbed by the vertebrate body and Mallory has shown its

presence in large amounts in the liver and other tissues in hemochromatosis.

It gains entrance to food most commonly by going into solution from copper or bronze containers. Mallory cites sources from copper stills used in the distillation of alcohol and large kettles employed in making apple butter and cider.

Copper sulphate is used to poison objectionable algæ in water. This causes the algæ to form a deposit on the bottom of the container and most of the copper is carried down with this sediment. Filtration will then remove all but a small amount of the copper and leave the water entirely potable and non-poisonous.

Copper sprays on leafy vegetables is a more important way in which considerable amounts of copper may be consumed because this metal possesses an affinity for chlorophyl. Adulteration of green vegetables with copper salts to give them a fresh appearance has been practised and Wiley cites the practice in other countries of using copper sulphate to enhance the color of canned green peas.

No absolute statement can be made as to the amount of copper poisonous to man but it is generally believed that the proportion of 0.1 to 0.25 parts per 1,000,000 of treated and then filtered water leaves no possibility of poisoning.

Absorbed copper is largely deposited in the liver but may be found in the kidney, spleen and thyroid. It is lost from the body by way of all of the excretions and is secreted in bile and milk.

Fluorine.—Many natural waters contain from less than 1 to 14 parts of fluorine per 1,000,000. The distribution of fluoride-containing waters is spotted geographically because of the scattered occurrence of fluorides in the earth's crust and the accessibility of these strata to the sources of the water supply. The latter factor is probably the more important because of the high prevalence of fluorine generally in the earth's crust.

It has been shown that fluorides are present to harmful degrees in both drinking water and water used for cooking so that these are both potential sources of poisoning.

The absorption of fluorine results in a toxicosis which has both general and local effects. According to Smith[1] there is a metabolic disturbance which results in the mobilization and loss of calcium giving a picture in rats much like rickets. This has not been demonstrated in the human although it may be that it occurs in a minimal degree.

The outstanding effect of this mineral is on the teeth and more specifically on the enamel formation of unerupted teeth. The mechanism of the interference with enamelization is not known but the result is a chalky softening of the enamel layer. This tends to appear in spots giving a mottled appearance. Smith suggests that

[1] Smith, M. E.: Am. Jour. Pub Health, 25, 696, 1935.

this peculiar effect is produced by intermittent intoxication, and she confirms her belief by producing alternation of chalky and normal enamel layers in the teeth of rats fed on a constant ration of food with intermittent introduction of fluoride into the diet. The number of chalky layers corresponded to the number of fluoride-food periods.

Because enamelization of the deciduous teeth is almost completed before birth these teeth are not as readily affected by fluorine. Recent work of Smith has shown that this is not a hard and fast rule for a mother who has consumed heavily contaminated water has been shown to present mottled enamel in the deciduous teeth of her offspring. It is believed that the placenta blocks the passage of low concentrations of fluorine but may permit large amounts to pass into the fetal blood.

It has more recently been shown that fluorine may influence the dentin of permanent teeth but not the enamel. This results in a hidden internal softening of the tooth.

Fluorine has lately been substituted for arsenic in vegetable sprays. The salts used are barium silico-fluoride and sodium-silicofluoride. Since mottled enamel has been found in areas where the water supply contained as little as 1 part of fluoride per 1,000,000, and since the U. S. Department of Agriculture determined the presence of 5.6 parts per 1,000,000 on apples three months after they had been sprayed and showed that washing cannot remove more than 80 to 90 per cent of the spray the quantity remaining may still be too near the minimal toxic concentration.

Aluminum.—The double salt of aluminum, aluminum-potassium sulphate or alum is widely used in baking powders but the amount possible for one person to consume from this source is far under that which may have any untoward effects. Poisoning from contamination of food is therefore hardly to be considered.

There is also no evidence to indicate that aluminum cooking ware can give up enough of this metal to produce poisoning.

Zinc.—The only suggestion that zinc may have any effect in man is Mallory's[1] contention that chronic zinc (and copper) poisoning results in the deposition of hemofuscin in the tissues. He believes that the source of this zinc is cooking utensils and apparratus used in the brewing industry. No statements can be made as to amounts which may be harmful. Mallory found hemofuscin only in adults over forty-five years of age.

Botulinus Toxin.—This is a powerful neurotoxin produced by *Clostridium botulinum.* The organism itself is a saprophytic anaërobe which grows readily in many common foods. The toxin is a specific exotoxin and appears therefore as a soluble poison in the food which has acted as the culture medium. The ingestion of such contaminated food results in the condition of intoxication called

[1] Mallory, F. B.: Jour. Med Res., 42, 461, 1921; Am. Jour. Path., 1, 117, 1925

botulism. This is a true exogenous chemical poisoning and not an infection.

Botulism toxin is the only true toxin absorbed from the gastro-intestinal tract of man.

C. botulinum is widespread in Nature as a common inhabitant of most soils, although its distribution, as judged by outbreaks of botulism, may not be equal and continuous.

It may be safely assumed that most foods are exposed to botulinus spores but that the organism grows only when the culture *medium supplied by the food is just right. The first requirement* of the organism is protein so that it can only grow in protein-containing foods. It is anaërobic and must therefore be protected from air and sunlight by being brought into the center of a foodstuff or enclosed in an airless container. For these reasons *C. botulinum* infection of food occurs most commonly in those instances where the food medium has been prepared in such a way as not to have destroyed the organism and under conditions that favor its growth. Such conditions are met most frequently in home canning and preserving, and occasionally in faulty commercial preparations.

C. botulinum spores are resistant to the ordinary cooking temperatures unless the heat is retained for some time. In the absence of other factors which may lower its thermal death point a temperature of 120° C. (248° F.) maintained for a minimum of ten minutes is necessary to kill the spores. This is above the boiling-point of water and may not be reached in home cooking unless the conditions of commercial preparation have been simulated by heating under pressure. Acidulation and the addition of glucose lower the thermal death point and since these are common practices in pickling and preserving they add to the margin of safety.

Another danger in home preservation of foods lies in the contamination of food after it has been cooked under the false assurance that the cooking has completely sterilized the food or prevented further changes in it. The ignorant custom of permitting cooked foods to stand around outside of the ice-box or in open cans at room temperatures is responsible for much botulism.

The foods most commonly involved are ham and pork products, *string beans, corn,* olives (mostly ripe), asparagus, spinach, peas, beets and more rarely other meats and sea-foods. This is not indicative of any special predilection of the bacillus for these foods but because the conditions under which they are prepared and handled are favorable to the organism.

Botulinus toxin possesses a curare-like effect. It produces an *ascending cord paralysis* and terminates in bulbar palsy. It is absorbed directly from the intestine, being resistant to the gastro-intestinal secretions, and exerts its first effect on the mesenteric

plexus thus involving the intestines early in its attack. Death results from respiratory center paralysis.

The onset of symptoms may appear within a few hours after the ingestion of the poison or may be delayed for several days. In general, the more rapid the onset, the more serious the results. The case fatality rate is seldom under 50 per cent and may be 100 per cent.

Wide discrepancies appear in estimates of the amount of poisoned food required to produce intoxication. This may be explained by differences in the intensity of toxin production, the strain of the organism, and possibly, individual factors. Rosenau records a dose of 0.000001 cc. which proved fatal to a 250 gram guinea-pig and a fatal case in a human after nibbling a portion of the pod of a spoiled string-bean.

Botulinus toxin is a true toxin as shown by its antigenic effect in producing a specific antitoxin in susceptible animals. Horse botulinus antitoxin can be obtained in sufficient titer to be useful in combating the poison in man. Since two toxic strains of *C. botulinum* are known (Types A and B) both should be used in the preparation of antitoxin.

(c) **Products of Food Decomposition.**—The ordinary decomposition products of organic matter are of little significance in poisoning. Objectionable gases and acids may arise during the processes of fermentation and putrefaction and make food less appetizing, and even nauseating, but they of themselves are non-poisonous. Indirect physiologic results may be conceded to follow the ingestion of excessive amounts of such products as lactic, butyric and other acids. They arise in food almost entirely from bacterial action.

The ptomains are a loose group of basic, nitrogenous cleavage products of the protein molecule, some rich and others poor in oxygen. They are: methylamin, di-methylamin, tri-methylamin, cadaverin, putrescin, muscarin, neurin, choline, betain and mytilotoxin.

Ptomains are non-specific and possess no antigenic properties (distinguishing them from toxins). They result from the action of several forms of bacteria on protein media, and one form of bacterium may produce different cleavage products under varying conditions such as presence or absence of oxygen, availability of protein other than amino-acids, temperature, reaction of media, and stage of the process when the organism is introduced.

Only two of the ptomains are looked upon today as harmful. They are muscarin and mytilotoxin. There is some doubt that mytelotoxin is the cause of food poisoning since the finding of another active poison in spawning mussels. Muscarin is however, one of the active glucosides in mushroom poisoning (see page 194).

"Ptomain Poisoning" as such is now dropped from the literature and is never used as synonymous with "Food Poisoning."

DEFENSE AGAINST POISONS TAKEN WITH FOOD.

The broad defense against this group of poisons is legislation. In the United States the U. S. Food and Drugs Act is the instrument under which the Federal Government administers its control over adulteration of foodstuffs and assures the marketing of only safe foods. This act is supported locally by State and Municipal Sanitary Codes.

It is quite impossible in most instances for the average consumer to detect adulteration or the addition of preservatives in harmful amounts. Furthermore, he cannot protect himself against contaminated food supplies unless they reveal themselves by some gross change in odor, taste, color or appearance.

Public opinion, through harmful notoriety, is a strong weapon against careless or fraudulent practices on the part of food merchants. Thus, the canners became convinced of the value of a clean product after the exposure of their infected foods was made public following a series of outbreaks of botulism. As a result the food canners have not been responsible for any series of botulism cases in the United States since 1925.

Technical advances in equipment have reduced the number of poisoning cases from arsenic, lead and copper. Lead pipes are being replaced by iron, lead solder by zinc, shellac lined containers by glass or some non-corroding metal.

More effective refrigeration in stores, homes and transport vehicles has added greatly to the safe preservation of food and largely done away with the necessity for chemical preservatives.

Although qualitative and quantitative adulteration still persists it is largely of the nature of cheap substitution of non-poisonous articles.

The widespread use of sprays in pest control has opened up a new and serious menace to health. If these useful but potentially harmful practices persist the agencies responsible for controlling them must keep an ever watchful eye upon them. Small scale fruit growers and vegetable venders can readily make use of these poisonous sprays and fail to wash and treat their products with sufficient thoroughness. In view of this popular practice hotel and restaurant keepers and housewives should be told of the potential dangers and instructed how to wash and clean produce bought in the public market; particularly that arsenic can best be removed by washing in slightly acidulated water.

The high fluorine content of water in certain regions is a problem of current importance as no method has been devised by which mottled enamel can be prevented among children who drink this water. The addition of calcium to the diet may aid in preventing

calcium loss but has not been shown to influence the local effect on the teeth.

Fluoride sprays and washes on fruits and vegetables should be prohibited.

Poisoning by contaminated food (other than by pathogenic bacteria) in the home is mostly due to botulism. The single defense against this disease is the use of only fresh or well cooked food. Fresh uncooked food will not harbor *C. botulinum* and well cooked food will destroy the spores of the organism. Home canning should only be undertaken by those with a good understanding of the principles involved and the facilities for carrying them out.

Foods laid aside for future consumption should always be kept at a low temperature in an efficient refrigerator, or if traveling, on ice. Prepared protein foods, which are not well salted or pickled and which have been allowed to stand unprotected at room temperature for more than a few hours should not be eaten. This applies to all meats, sea-foods, dairy products, and many green vegetables such as beans, peas, asparagus and corn.

Sausage meat, the food in which *C. botulinum* was first demonstrated, still remains the chief offender.

CHAPTER XVIII.

POISONS ACQUIRED BY INGESTION (Continued).

POISONS TAKEN AS MEDICINES.

The harmful effects of drugs and medicines are here considered only as they are prescribed by a physician, or taken under legitimate direction. This section does not consider medicines taken in poisonous amounts by accident or with harmful intent.

Although most medicines *may produce poisonous effects they* are not necessarily poisonous. The physiologic action of all drugs is of the nature of a chemical (or physico-chemical) exchange between themselves and the tissues on which they act. Any poisonous qualities which they possess become manifest only when the changes they produce disturb the tissue or cell mechanisms beyond their limits of tolerance.

It is impossible to know at present the limit of tolerance of the tissue cells that are acted upon by a given drug, nor can the circumstances under which it may reach this limit be measured with certainty. The sciences of pharmacology and therapeutics have examined all drugs and medicines now in use and have established an average range of dosage for each.

The amounts that they have prescribed express the average dose of each that will, on the average, produce no harm but will be sufficient to bring about its desired effects.

Poisoning from legitimate medication results from failure to evaluate either the limit of tolerance or the circumstances under which the drug is administered. Not infrequently the safe limit is greatly reduced without the physician being aware of it and poisoning results from a dose considerably below the average. On the other hand an ordinarily safe dose may *be enhanced in its effect by excessively* rapid absorption, or delay in its elimination may permit it to act over an unsafe period of time.

Some drugs possess a cumulative action, that is their physiologic effect is prolonged or they continue to exert their effect long enough *to overlap the added effect of subsequent* doses. *Digitalis*, quinine, arsenic, lead, mercury and the iodides are outstanding examples. In these, there is either a delay in their elimination or they may be actually stored in the tissues.

The tolerable amount of some drugs bears an important relationship to body weight. It is due in all probability to the diluting

effect of the body fluids and tissues. Any given amount of a drug which is carried generally throughout the body will necessarily reach a given tissue in more dilute form in a large body than in a small one. This does not apply in instances where the drug reaches its selective tissue without entering the circulation, as in the case of locally acting respiratory or gastro-intestinal medicaments.

The above consideration along with the accelerated growth processes and tissue immaturity of young children leads to the general rule, that children can tolerate only a fraction of the adult dose. According to Young's formula the dose for a child is the fraction of the adult dose represented by $\frac{\text{age}}{\text{age } 12}$. This formula cannot be more accurate than the dosage for the adults and for certain drugs does not hold at all. Opium given according to the Young formula would be in too great an amount for a child and many of the purgatives and laxatives would be ineffectual.

The toxicologic effects of drugs may be exaggerations of their therapeutic action or the results of secondary effects unrelated to their pharmacologic action. Thus, strychnine poisoning is produced through the same mechanisms that are involved in its non-toxic therapeutic action whereas the bromides in overdose produce acne, mercury causes stomatitis or renal damage, and arsenic produces dermatitis.

The undesirable effects frequently occur before the drug has been able to produce its optimum pharmacologic action. It is not uncommon to find instances in which the desired effect of quinine or emetine cannot be reached before the onset of unfavorable reactions. Undoubtedly many therapeutic failures result from this cause and poisonings occur in an attempt to push the drug in spite of these undesirable results. Poisoning may result therefore from overzealous therapy on the part of a physician or through self-medication by the public. In some instances the physician may permit mild toxic effects when he feels that the advantages of the medication outweigh any possibility of permanent damage from the heavy dosage. This is none the less true intoxication although it is deliberate. The lay public on the other hand cannot separate the toxic from the therapeutic effects and may suffer irreparable harm from unintelligent use of home remedies. To the layman the directions on the label appear to be dependable and acting the on assumption that "if a little does good, a lot will do more good" opens himself to opportunities for serious poisoning.

Harmful ingredients may occur in patent and proprietary medicines which have been permitted on the market through oversight or carelessness or deliberate fraud contrary to the provisions of the Food and Drugs Act. Of recent interest is the use of diethylene glycol as a solvent for sulfanilamid which produced some 70 or more

deaths in the United States in 1937. Many glycols (ethylene glycol, diethylene glycol, ethyl diethylene glycol or carbitol, ethyl ethylene glycol or cellosolve, 1–4 dioxan) are used as solvents for cellulose and resins and by pharmaceutical houses as solvents or vehicles for various resinous drugs. Ethylene glycol is a constituent of an anti-freeze mixture for automobile radiators and diethylene glycol is used in the treatment of cigarette papers.

The derivatives of ethylene glycol have been found by von Oettingen and Jirouch[1] to possess various toxicities depending largely on the manner in which they are administered. As a group they produce muscular and nervous depression, hemolysis, and nervous depression. Kesten, Mulinos, and Pomerantz[2] find that diethylene glycol in poisonous amounts in rabbits produces a severe hydropic degeneration of the convoluted tubules of the kidney and to a lesser extent of the liver and adrenals. Human deaths from diethylene glycol used as a solvent vehicle in place of glycerine to carry sulphanilamid in solution have resulted from kidney damage and anuria.

Hansen[3] has reported severe poisoning from drinking anti-freeze mixture containing ethylene glycol.

Every therapeutic agent has its own particular mode of action and whether its effects are direct or indirect it brings them about through its own peculiar action on mechanisms susceptible to it. The consideration of the circumstances under which each drug acts and the mechanisms in which it is involved is beyond the space allotted in this work. For full particulars on the poisonous action of special drugs and therapeutic agents the reader is referred to standard works on Pharmacology, Therapeutics and Toxicology.

POISONS TAKEN AS DRUGS THROUGH ADDICTION.

There is no satisfactory definition of drug addiction or a habit-forming drug. If tolerance is taken as a criterion for addiction it is necessarily inaccurate because of the lack of understanding of what constitutes tolerance. Those substances showing symptoms on their withdrawal constitute the category of harmful habit-forming drugs according to some. The term narcotic drug addiction is obviously a restricted application.

It is necessary therefore to be arbitrary in the selection of drugs falling under this category. Those considered here will be the drugs and medicines accepted by common usage as having a strong tendency to bring about dependence on them for their effects.

[1] Von Oettingen, W F., and Jirouch, E. A.: Jour. Pharm and Exper Therap, 42, 355, 1931

[2] Kesten, H. D, Mulinos, M. G., Pomerantz, L.: Jour. Am Med Assn, 109, 1509, 1937.

[3] Hansen-Sammlg. Vergiftgs Fälle. I. A.: 175, 1930.

No undue importance will be laid on their physiologic necessity once the habit has been acquired, although this is unquestionably one of the main perpetuating factors.

At the basis of all of the more serious drug addictions lies the important factor of psychic necessity. That is, whether it be the psychopath's craving for release from his responsibilities, the sleepless neurotic's need for a hypnotic, the relief from pain for a chronic neuralgic, or the "courage" required by the mental and emotional inferiors, there is for each a reason why it should be taken which *arises out of some real or imagined need.*

An analysis of the causative factors of addiction must make a distinction between the predisposing, precipitating and continuing causes. What causes an individual to take up a habit-forming drug may be quite different from the reasons for continuing it. A single case may be cited to show these distinctions. A young girl who was given paregoric for dysmenorrhea recognized the same feeling of relief on a later occasion when she was given a hypodermic of morphine for a fractured leg. Previous to the accident she had not known that paregoric was an opiate but when she was informed of the connection between paregoric and morphine she soon switched over to the use of morphine for her dysmenorrhea. Within three months she was using morphine tablets for relief from the worries of a love affair and when she was seen by the writer some years later she was a physical and mental wreck, accustomed to her daily "shots" and almost maniacal in her demand for morphine. The initiating and continuing factors in her case were distinctly different but each involved a psychic need.

This brief introduction will serve to emphasize the joint action *of psychic and poisonous factors in the natural history of drug* addiction. It is the poisonous substances themselves with which this section is most concerned.

The commonest habitually ingested poisons are alcohol and caffeine. These common beverages have been considered in the preceding sections.

Opium and Its Derivatives.—Opium and its derivatives is looked *upon as the type drug in the category of drug addiction. Outside* of the Orient it is generally taken by mouth at the beginning of addiction but there is a strong tendency to use it in hypodermic form by those well established in the habit.

Preparations and extracts of opium taken by mouth are paregoric (Tr. Opii camphorata), laudanum (Tr. Opii), Sydenham's laudanum (Vinum opii), black drop (Acetum opii), Dover's powder (Pulvis opii et ipecacuanhæ) pantopon (Pantopium hydrochloridum), morphine sulphate and hydrochloride, Tully's powder (Pulvis *Morphinæ Compositus), codeine (Methylmorphine) and heroin* (Diacetylmorphine).

The alkaloids of opium and their salts are absorbed directly by the gastric and intestinal mucosa. Their presence in the alimentary tract produces no local action but after absorption they exert a profound effect on the gastro-intestinal musculature. According to Cushny they have been shown to produce reduced tonicity of the gastric musculature and increased tone with spasticity of the muscles of the colon. The former delays the emptying time of the stomach and the latter holds the fecal contents longer in the large intestine. The two together permit more efficient digestion of food and greater absorption of the digested and fluid portions. The relatively small amount of residue and the disturbance of peristalsis result in a sluggish bowel and constipation. Denervation of the intestine does not alter this condition so that the constipation is not due to any nerve effect of morphine.

In its passage through the blood stream, morphine (as all other narcotic opium alkaloids) influences the cells of the central nervous system and shows a selective action on the respiratory center and the pain perception mechanism. The respiratory center in the medulla is depressed and respiration is slowed. In the sensorium the action is complex and not well understood. The manifestations of its effects are inability to concentrate, dulling of the pain response to continued stimuli, some loss of psychic inhibition and a resultant tendency to volubility, and a freer flow of the imagination. There is no explanation for this reaction other than by chemical change and altered function of the cells of the coördinating and mental associative mechanisms. The apparent increase in mental activity may be only a compensatory phenomenon in which higher brain centers are permitted temporary dominance over the lower because the latter no longer transmit the importunate impulses coming from the surface areas.

Morphine is partially oxidized in the body and some undergoes methylation, probably in the liver. The greatest part is eliminated in the urine, some escapes through the stomach walls and appears in the feces, and a part is stored for variable lengths of time in the general musculature. There is no evidence of antitoxin production or any special mechanism produced by the body to deal with it. If morphine is given in repeated doses (especially in large doses) it is soon found that the toxic effects do not follow unless the amount of the drug is increased. This is evidence of tolerance, but there is no satisfactory explanation for its development. Tolerance is probably a combination of many factors of which those mentioned are only part explanations.

When an individual who is habituated to opium is deprived of it or ceases its use he presents what are called withdrawal symptoms. These are mental agitation, worry, anxiety, depression, diarrhea, weak pulse, muscular pains, and psychic changes that involve the

personality to such a degree that an originally sound minded, sober individual becomes a depraved slave to any means that will gain his end, which is more morphine.

No satisfactory explanation for the withdrawal symptoms has been found. An alleged toxic product developed from or on account of morphine, has been hypothetically accepted by some but never demonstrated.

With the establishment of tolerance it is possible for a man to continue to use opium at an established level without suffering from any known pathologic effects. This is observed in the Oriental who smokes opium habitually, maintains his nutrition, and enjoys good health. Most, if not all of the harmful effects of opium in the habitue, are due to such associated factors as unavailability of the drug, worry over exposure of the habit, loss of appetite and the surrender of personal care, responsibility and interest to the needs created by the habit. Cases are recorded of addicts who habitually took 20 grains of morphine a day without serious effects. An average addict may stabilize his habit at 1 or 2 grains and continue his daily life unimpaired in mind or body. Some professional men are in this class and even their closest friends are unaware of the fact that they take the drug.

Heroin is more poisonous than morphine. Cushny states that its action is similar to but stronger than morphine in its effects on the cerebrum and medulla but that it has little effect on the intestine. Habituation to its use is readily acquired but it appears to be less well tolerated than morphine, especially in large doses. Mental deterioration is rapid and excessive in most heroin addicts.

Codeine is so little habit forming if at all that it is not included in the list of drugs under the U. S. Federal Narcotic Law. That a few instances of alleged addiction to codeine have been reported and some evidences of tolerance have been demonstrated, makes it necessary to question the advisability of looking upon this drug as completely non-habit forming. It is much weaker than morphine but slows the respiration and depresses the cerebrum in the same way.

Paraldehyde.—Carver, in a review of narcotic addictions expresses his belief that addiction to paraldehyde is on the increase. This he attributes to its common association with alcoholism.

Paraldehyde is a polymer aldehyde of acetylaldehyde, and possesses a disagreeable ethereal odor and a burning taste. The large amounts, 1.3 to 5 cc., required to produce the minimal effects, coupled with the undesirable qualities of taste and odor tends to reduce its general use.

In therapeutic doses it is a soporific and nervous sedative and when taken in large amounts produces a profound and often prolonged narcosis and unconsciousness.

It is used mostly for relief from alcoholic hangovers. Tolerance for the drug is rapidly reached but as rapidly lost and its withdrawal does not produce imperious craving for more, as in morphinism.

Chloral Hydrate.—Chloral hydrate is a soporific drug which first affects the cortical intellectual centers and then, in order, the motor cortex, motor side of the cord, motor nerve, and in heavy doses the sensory mechanisms.

Because of the early involvement of the higher functions of the brain its greatest use is for the production of narcosis to combat insomnia from mental causes. It is not used as an analgesic against pain.

Habituation to its use occurs under repeated necessity for relief occasioned by worry and anxiety. Chronic poisoning from its long use results in a weakening of the will and general physical depression. Cardiac and vasomotor weakness is concomitant with the general decline. Death from a single large dose is due to depression of the vasomotor center and its direct paralyzant effect on the heart muscle. The therapeutic dose is 0.6 to 1.3 grams, the average lethal dose is 10 grams. Recovery has followed after 3 or 4 times the last amount.

Sulphonal, Trional and Tetronal.—The members of this group of mildly soporific medicines are closely related pharmacologically to chloral. Sulphonal is sulphonmethane; trional is methylsulphonal. They act primarily on the brain as somnifacients but do not depress the heart. Because of their wide popularity in functional insomnia they have been subject to much abuse and the nervous individual is prone to continue their use through habit. Tolerance is acquired toward them and the need for fuller doses carries the user dangerously near or into poisonous amounts.

Sulphonal taken over a prolonged period produces a chronic state of weariness and unsteadiness of gait. This last may progress to a stage of paralysis. Early gastro-intestinal symptoms are common complaints.

The drug is slowly destroyed in the body by decomposition with the formation of ethylsulphonic acid. Because of the slowness of this process cumulative effects may occur if its use is long continued.

Sulphonal possess the peculiar property of decomposing hemoglobin with the liberation of hematoporphyrin an iron-free pigment. This is excreted by the kidneys and gives a port wine color to the urine (hematoporphyrinuria).

The lethal effect of prolonged addiction to sulphonal is brought about by respiratory paralysis or suppression of the urine.

Trional and tetronal are similar to sulphonal in their physiologic and toxicologic action.

The Barbiturates.

Barbital; (Veronal)—diethylbarbituric acid.
Phenobarbital; (Luminal)—phenyl-ethyl-barbituric acid.
Sodium barbital; (Medinal)—soluble barbital.
Allonal; allylisopropylbarbituric acid (with amidopyrine).
Amytal; iso-amyl-ethyl barbituric acid.
Dial; di-allyl barbituric acid.

The salts and compounds of barbituric acid were introduced to medicine as soporifics and central nervous system sedatives. New combinations have continued to appear, each one alleged to possess more specific pharmacologic properties and less toxicity than the others. Nevertheless, as a group, they have all been shown to produce harmful effects when continued over too long a time. They are slowly eliminated and thus may show cumulative effects with continued dosage.

Barbital may not be eliminated for two or three days after ingestion and 70 to 80 per cent of it is lost unchanged through the kidneys. Barbital sodium is more soluble than barbital and is therefore more quickly and readily absorbed from the alimentary tract.

The barbiturates are sensory center depressants and narcotics. They are therefore indicated and used in the same group of functional nervous disorders as the chloral group of drugs. Luminal, in addition, is especially useful in epilepsy.

The margin of safety between the therapeutic and toxic doses is great so that acute poisoning occurs only after massive doses. Prolonged use however may cause serious intoxication. They are especially harmful to the kidneys in prolonged dosage so that they are contraindicated in the presence of renal disease.

Chronic poisoning is partly the result of the absolute quantitative amount of the drug consumed and in part due to the presence in the individual of an idiosyncrasy or hypersensitiveness to it. All of the barbiturates produce mental dulness. Prolonged use causes memory disturbances, slow cerebration and delayed associated responses as evidenced by speech defects and an ataxic gait. The temperament side of the personality may be altered in the direction of irritability and irrational outbursts.

Cyanosis is not infrequent and an increasing number of erythematous skin reactions are being reported.

Excessive dosage results in death from respiratory failure. It is preceded by cyanosis, coldness of the skin, depression of temperature, stupor and coma.

The Laxative Habit.—The widespread prevalence of constipation has always led to the use of a variety of home remedies and proprietary drugs for its relief. Although these medicines do not possess any habit-producing properties within themselves people get dependent upon them to "keep their bowels regular."

Few of the laxatives can be depended upon to continue their effect satisfactorily over a prolonged period of time because the mechanisms concerned become refractory to them or abnormal changes in the physiology of the digestive tract interfere with their effect. Some, such as phenolphthalein, may be definitely harmful in continued doses.

The habitual use of the same laxative is to be condemned for these reasons alone, if not for the more serious possibility that organic disease may be overlooked by attempting to treat one's self without the advice of a physician.

DEFENSE AGAINST MEDICINAL POISONS TAKEN BY MOUTH.

The uncertainty surrounding the absorbability of many pharmaceutical preparations and consequently the lack of any absolute knowledge of the dose received, the problem of idiosyncrasy and drug hypersensitiveness, and the possibility of toxic side-effects, make it imperative that the prescribing physician understand thoroughly the chemical nature and toxic action of his medicines and take into consideration the individuality of his patients. The newer synthetic drugs are especially dangerous when used without full knowledge regarding them and physicians must be warned not to accept the claims of salesmen and advertisements extolling their virtues. Chemical analyses and pharmacologic studies upon them are available in the reports of authoritative medical councils and should always be consulted.

Unfortunately, poisoning still occurs from the careless use of such standbys as digitalis, arsenic and strychnine, even when given over a physician's signature and according to his directions. His prescription may have been filled to the letter but the dose may have been wrong either because it was carelessly calculated or written or because it had not been adapted to the particular patient.

It is not uncommon for a doctor to prescribe a drug and fail to inform the patient how long he is to continue its use or thoughtlessly to allow the patient to get the prescription refilled without first checking up on the results of the first supply. Many cases of drug addiction can be found to have their onset in faulty medication. *All habit-forming drugs should be dispensed in small amounts, and if necessary, in disguise.* Awareness of the potentiality for habit production in an emotionally unstable or intellectually weak individual should be a warning against casualness in their use.

The limitations in the supply of narcotics available to the public throws much of the responsibility for continuation of the narcotic habit on the medical practitioners to whom the addicts come to obtain the drug. Early addicts and those who have stabilized their dosage present little evidence of their addiction and the subjective

symptoms which they present cannot be disproven. It is easy to be misled by their subterfuge and so aid unknowingly in the perpetuation of the habit.

The Harrison Narcotic Act in the United States and similar acts in other countries aim to reduce the supply and use of illegal narcotic drugs by placing restrictions on their importation, sale and possession. In the United States a physician who prescribes a narcotic knowingly to an addict is liable to punishment by imprisonment. He can only prescribe them under any conditions by possessing a special narcotic license. A record must be kept of the amounts used and for whom prescribed.

Education must largely be relied upon to prevent the ever-increasing use of medicines without medical supervision. Printed advertisements and the radio carry on a campaign of deception over the virtues of the commodities which they represent. The use of the term "scientific" as applied to the authority for their products is not only untrue but is the current psychologic catchword that impresses the people with its spurious authority. Qualifying statements required by law on labels and packages are so disguised by wording, size of type and other deceitful practices that they are seldom seen or read.

The esthetic senses are appealed to by incorporating harmful medicines in chocolate covered candies, chewing gum and beverages, thus giving them an especial appeal to children and finicky adults.

People must be taught that home medication is dangerous; that few medicines do all that they are claimed to do; that some preparations have no medicinal value whatsoever; that they cannot judge what medicines are needed in particular instances; that the long-continued or habitual use of innocent drugs may be harmful.

The National Food and Drugs Act, the Radio Commission and Advertisers Associations can do much to prevent the dangers of harmful drugs, but the deeper, more fundamental requirement is an understanding by the public that it is being exploited. The physicians must fight misrepresentation and ignorance all along the way.

CHAPTER XIX.

POISONS ACQUIRED BY INGESTION (CONTINUED).

POISONS TAKEN BY MOUTH THROUGH ACCIDENT OR CARELESSNESS.

MANY highly poisonous substances are found as ingredients of common household supplies. These, through mistakes in identity, ignorance as to their use, carelessness in marking their containers, and leaving them where they may fall into the hands of children and infants are a prolific source of accidental poisoning. Aikman[1] reports that more than 500 deaths from acute poisoning (gas excepted) occur yearly in the United States in children under five years of age. There were 1605 deaths in all ages from accidental poisoning (gas excepted) in the United States in 1932. The relatively high number of deaths under five years (over one-third of the whole) is evidence that many deaths from this category must be preventable.

The average home medicine closet or shelf is usually found stacked with home remedies, partly consumed prescription medicines in bottles and boxes, iodine and other first aid preparations, cosmetics, irrigating solutions or tablets for making them up, and sundry cleaning and household supplies in bottles or jars not unlike their medical counterparts or actually kept in old prescription bottles. Frequently the original labels on the latter have not even been removed or changed to designate their new contents.

The hall and kitchen closets are repositories for insect and vermin eradicators, various polishes for the floor, furniture, kitchenware and table utensils, bleaches and blueing for the laundry, drain and sink openers and toilet and washbowl cleansers.

Anywhere about the house, workshop or barn may be found numerous chemical compounds such as ink eradicators, photographic materials, workshop supplies, weed killers, fruit and vegetable sprays, liniments for man and animals, shoe, harness and metal polishes, lye, kerosene and gasolene.

Most of the adult accidental poisons come from the medicine closet or kitchen self. In the first instance they are frequently picked up and used without first having identified the bottle, or they may be taken for a medicine bottle in which they had been placed without proper labeling. Among the common mistakes occurring in this way are the use of iodine in place of some dark

[1] Aikman, J.: Jour. Am Med. Assn., 103, 640, 1934

liquid medicine such as fluidextract of cascara, bichloride of mercury tablets for aspirin, mercurial douche concentrates for liquid prescriptions, phenol and cresol compounds for cough mixtures, and *boric acid for sodium bicarbonate. Some serious poisonings have* occurred because the victims were so sure they "knew just where the bottle stood" that they picked up the bottle occupying that place in the dark and drank it without turning on the light.

On the kitchen shelf, rat and vermin powders have been placed in baking powder tins and cereal boxes and so used in cooking. A series of poisonings occurred in Philadelphia in which such a mixture had been placed on a grocer's shelf and sold over the counter.

The following list of poisonous substances found in household and workshop supplies is taken from Aikman's excellent article:

POISONS FOUND IN INSECTICIDES, RODENTICIDES AND FIREWORKS.

Roaches, Ants, Fleas and Crickets:
- Pyrethrum
- Sodium fluoride
- Paris green
- Thallium

Bedbug, Fly and Mosquito:
- Cresol
- Phenol
- Pyrethrum
- Naphthalene
- Nicotine

Rodents: Rats, Mice, Moles, Gophers, Woodchucks:
- Cyanid
- Arsenic
- Phosphorus
- Thallium sulphate
- Red squill
- Sulphur
- Yellow phosphorus
- Formaldehyde
- Hydrocyanic acid
- Chloropicrin

Fireworks:
- Mercuric sulphocyanid
- Arsenic sulphocyanid
- Phosphorus ("spit-devil" or ' son-of-a-gun")
- Mercury in victory snakes

Poisons in Paints:
- Lead:
  - White lead
  - Chrome yellow, orange and green
  - Glazes, enamels, putty
  - Spray paints, lacquers, enamels
- Arsenic:
  - Sheel's green
  - Emerald green
- Benzene (C_6H_6):
  - Quick drying paints
  - Spray paints, lacquers, varnish
  - Paint removers, shellac, stains
  - Covering for automobile tops
  - Bronzing and gilding fluids
- Methyl Alcohol and Denatured Alcohol:
  - Varnish and shellac
  - Varnish and paint removers
  - Solvents for gums, dyes, resins
  - Coatings containing cellulose nitrate

POISONS FOUND IN INSECTICIDES, RODENTICIDES AND FIREWORKS.
(Continued.)

Poisons in Paints:—
- Naphtha
- Benzine
- Turpentine
- Anilin

Cosmetic Preparations:
- Freckle removers:
  - Corrosive mercuric chloride
  - Ammoniated mercury
  - Bismuth
- Mole and wart removers:
  - Acids or caustics (see Caustic Poisons)
- Skin foods and creams:
  - Mercury
  - Salicylic acid
  - Lead
- Hair tonics and Dyes:
  - Lead
  - Sulphur
  - Silver salts
  - Pyrogallol
  - Bismuth
  - Arsenic
  - Salicylates
  - Anilin derivatives
- Deodorants:
  - Solution of an ammonium salt (practically harmless)
- Depilatories:
  - Barium or sodium sulphate
  - Thallium acetate

Caustic Poisons:
- Hydrochloric acid:
  - Tinner's acid (for mixing soldering fluid)
  - Hand and toilet bowl cleaners
  - Sink cleaners
  - Weed killers
- Sulphuric acid:
  - Acid for refilling fire extinguishers
  - Electrolyte for lead storage batteries
  - Metal cleaners
  - Toilet bowl cleaners (acid sodium sulphate)
- Nitric acid:
  - Metal cleaners
  - For wart removal
- Phenol (Carbolic acid):
  - Carbolic disinfectant soaps
  - Coal-tar disinfectants and dips
  - Carbolated petrolatum and oils
  - Toothache remedies and other dental preparations
- Oxalic acid and its salts:
  - Metal and wood polishes
  - Straw hat cleaners
  - Photographic materials (blue print and platinotype products)
  - Ink removers
  - Rust remover
  - Bleaching preparations
  - Soluble laundry blue

POISONS FOUND IN INSECTICIDES, RODENTICIDES AND FIREWORKS. (*Continued.*)

Caustic Poisons:—
- Acetic acid:
  - Ink eradicators
  - Photographic hardeners
  - Shoe polishes
  - Metal polishes
  - Wart removers
- Potassium and sodium hydroxide:
  - Potash or lye
  - Paint and varnish removers
  - *Washing and cleaning preparations*
  - Dehorning preparations
  - Sink and drainpipe cleaners
  - Electrolyte for Edison storage batteries
  - Manicuring preparations
- Silver nitrate (lunar caustic):
  - Wart removers
  - Hair dyes
  - Silver polishing and plating compounds
  - Intensifiers for photographic work
  - Indelible marking inks
- Ammonia:
  - Ammonia water
  - *Household ammonia*
  - Cleaning compounds
  - Hartshorn liniments
  - Hair-waving solutions

Poisonous Plants.—There are a number of plants whose seeds, leaves or flowers possess toxic properties and which are occasionally eaten through accident. Children especially are prone to eat these attractive articles.

Many varieties of the common crow-foot (gen. *Ranunculus*) have succulent leaves which contain an irritating juice which when eaten produces pain and spasm in the esophagus and severe abdominal cramps. As little as 2 drops of the expressed juice may produce poisoning and one flower will produce the same effect.

The flower of *Anemone pulsatilla* causes vomiting.

Marsh marigold (*Caltha palustris*) contains a highly irritating acrid poison. Five members of a family reported to have eaten marigold by accident suffered general intoxication with abdominal pain, ringing in the ears, headache, diarrhea and generalized edema.

Delphinium staphysagria produces local inflammatory lesions in the stomach and in experimental animals (dog) has caused fatal poisoning with general paralysis and convulsions.

Elaterium, one of the *cucurbitaceæ*, contains an active principle, elaterin, which in amounts as small as one-tenth grain may cause purging.

The bean of *Ricinus communis* (castor-oil bean) is highly toxic,

three seeds having proved fatal to an adult. The active principle, ricin, is a true phytotoxin, in that it acts as an antigen and causes the production of antibodies. Almost all varieties of ricinus seeds yield hemo-agglutinins. Ricin causes agglutination of the erythrocytes, local cellular destruction and hemolysis.[1] The ingestion of castor-oil beans produces vomiting, purging, abdominal pain and prostration.

Daphne mezereon berries are beautiful and attractive to children but are very poisonous. The bark of the plant contains the active principle (daphnine) in greater amounts. It causes abdominal cramps, bloody vomiting and diarrhea, which, if not fatal, may persist for several weeks.

Daffodils (*Narcissus pseudonarcissus*) are mildly irritating to the stomach and intestines.

The spotted hemlock (*Conium maculatum*) resembles parsley and has been used by mistake for this garnish. It produces dryness and tightness of the throat, prostration, dilation of the pupils, convulsions, delirium and coma.

Laburnum (*Cytisus laburnum*), and privet (*Lagustrum vulgare*) are common ornamental bushes, the leaves of which may be consumed by children. They both possess irritant principles which may show narcotic effects even in small amounts.

Hibiscus (*Hibiscus*) flowers are powerful gastric irritants and general depressants.

Prussic or hydrocyanic acid may be formed from amygdalin or its compounds in the presence of water, from the following plant products:[2] bitter almond seeds (*Amygdala amara*); cherry laurel (*Prunus laurocerasus*); plum kernels (*Prunus domesticus*); bark, leaves and flowers of the wild Service tree (*Prunus padus*); the bark of wild cherry (*Prunus virginiana*); flowers and kernels of *Prunus aucuparia; S. hybrida* and *S. torminalis;* young twigs of *Cratægus oxyacantha*, leaves, and flowers of shrubby Spiræcæ such as *Spiræa aruncus, S. sorbifolia*, and *S. japonica;* the roots of the sweet and bitter cassava. Peach kernel contains 2.85 per cent amygdalin and apple pips 0.6 per cent.

The leaves of *Aconitum napellus* resemble salad and the roots simulate horseradish to the extent that they have been eaten by mistake for these vegetables. The poisonous effects are due to the powerful alkaloid aconitine. Aconite, or monk's-hood, is frequently grown in flower gardens because of its attractive hood-like flowers. Seeding of the plant among nearby vegetables makes it readily possible for the early plant to be mistaken for an edible food.

Aconitine produces numbness and tingling in the mouth. It is a

[1] Wells, H G Chemical Pathology, Philadelphia, W. B Saunders Company, 1925

[2] Emerson, R L Legal Medicine and Toxicology, New York, D Appleton & Co., p. 315, 1909

powerful depressant of the perceptive centers of the brain, sensory side of the spinal cord and peripheral ends of the spinal nerves. It is also a vagus center stimulant and heart-muscle sedative. In large doses it depresses the vasomotor center. The combined action results in fall in blood-pressure and slowed pulse-rate. Respiration becomes slow and shallow. Death results from cardiac arrest in diastole.

Calabar bean, the fruit of *Physostigma venenosum,* has caused accidental poisoning in children. The principal alkaloid of this bean, physostigmine or eserine, produces weakness of muscles with involuntary twitching, diarrhea and vomiting, respiratory embarrassment, and excitation of the central nervous system with ultimate exhaustion. Death of a boy has been reported from the ingestion of six beans.

The common horse-chestnuts, *Æsculus hippocastanum* and *A. pavia* contain a glucoside, æsculin which is a bitter and astringent carminative. In the United States deaths with convulsions in children are reported from eating the nuts of this ornamental tree.

Holly berries (Ilex aquifolium) possess irritating and narcotic properties even in small amounts.

Helleborus niger (the Christman rose), *H. viridis,* and *H. fœtidus* are all poisonous, due to the action of the glucosides helleborin and helleborein. These substances are more abundant in the roots, and it is from decoctions of these that deaths have occurred. Poisoning resembles that of digitalis and death occurs from its action on the heart.

The leaves of oleander also contain a digitalis-like poison from which deaths have been reported. One at least of the active substances has been named neriin from the generic name of *Nerium oleander.*

Fool's parsley or *Æthusa cynapium* is a plant much resembling parsley and has been mistaken for it with poisonous results. The leaves however are black on the under surfaces and when bruised emit a nauseous smell. It produces nausea, vomiting and gastrointestinal irritation.

Colchicum autumnale or meadow saffron grows wild and causes many deaths among cattle. The entire plant is poisonous but accidental poisonings are more common from consumption of the seeds or corms by children.

The harmful active ingredient is the alkaloid colchicine. Ingestion of the seeds (and also other parts of the plant and preparations made from them) produce burning pain in the stomach, vomiting, diarrhea and bloody stools if the dosage has been high. Death may occur with convulsions, stupor, a soft thready pulse, subnormal temperature and collapse.

The poisonous thorn apple is *Datura stramonium.* Although the dangerous alkaloid hyoscyamin is present in all parts of the plant

it is from the seeds within the prickly fruit that poisoning mostly occurs. It is usually accidentally acquired by children.

Hyoscyamin is a strong cerebral depressant and in poisonous doses produces deep sleep or coma. On the heart it causes acceleration by paralysis of the inhibitory terminations. Delirium results from heavy dosage. Death is not common but is more likely to occur in children and feeble persons.

DEFENSE AGAINST ACCIDENTALLY INGESTED POISONS.

Over three-fifths of the accidental poisonings in children occur during the runabout years. At that time they are about and into everything within reach and have not yet attained an age when they can reasonably be instructed with much assurance of being obeyed. Their propensity for satisfying their curiosity by taste adds to the hazard of leaving poisonous substances within their reach. Medicines should always be kept on a high shelf or in a lock closet which should be kept locked. The poisonous household supplies should also be kept in places inaccessible to children.

Outstanding among the medicines attractive to children are the highly colored laxative tablets containing strychnine. A child may readily scoop up a handful of these and obtain a fatally poisonous dose of strychnine.

Although the proper labeling of poison-containing articles is and should be required by law the main defense within this category is against carelessness on the part of adults. No amount of poison labels can be effective against the ignorant use of substances taken in the dark or left within the reach of children. A sop has been given to carelessness by placing highly poisonous medicines in oddly shaped bottles which can be identified by touch in the dark or by hanging little bells around the bottle neck to give a warning tinkle when it is picked up.

Physicians can aid by prescribing smaller amounts of poisonous drugs so that there will be little or none left after the requisite number of doses have been taken and by relying on refills for continued treatment. They can also be an important educational factor in the homes of patients by calling their attention to harmful practices coming under their observation. Probably also, many old time remedies need not be prescribed at all.

It is almost too obvious to say that small children should be taught not to eat leaves and flowers of plants and yet as shown above, the number of accidental poisonings from this source is not inconsiderable. Children *can* be taught not to do certain things and the faulty habit of putting everything in the mouth is one of them. Intelligent training, even in the young child, is the logical prevention in this instance. Adults too can be told of the dangers inherent in certain plants and plant products.

CHAPTER XX.

POISONS ACQUIRED BY INGESTION (CONCLUDED).

SUICIDAL AND HOMICIDAL POISONS.

ALTHOUGH the individual with suicidal or homicidal intent may not find it easy to obtain his poison of choice, or the uninformed may not get a rapidly fatal type or amount of the poison which he wants, there are always many death-producing poisons available in the open market. They are sold as medicines or therapeutic agents of some kind or are common articles in the trades. Few of them have restrictions on their sale which are effective enough to prevent anyone from buying them in sufficient quantities to cause death. Where an agent may sell only a limited supply to any one individual there is seldom anything to prevent the purchaser from going to more than one salesman.

The poisons leading the list for both homicide and suicide are arsenic and opium, each of which is responsible for approximately one-third of the deaths. Suicides commonly employ next in order, bichloride of mercury, carbolic acid, prussic acid and the cyanids, chloral hydrate, strychnine, aconite, physostigmine, chloroform and wood alcohol (methanol).

Homicides prefer prussic acid and the cyanids, muriatic acid, strychnine, chloral hydrate, oil of cedar and wood alcohol.

Other less common agents are phosphorus (generally obtained by soaking off match-heads), soldering salts, barbiturates, oxalic acid, iodine, ammonia water, turpentine, carbolic acid, oil of mustard, hemlock, creosote, kerosene and shellac.

There were 3320 suicides in the United States in 1932 "by the use of solid or liquid poisons or by absorption of corrosive substances" as against 1927 homicides (largely poisonings) "by means other than firearms and cutting or piercing instruments."[1]

Although the means of suicide vary in different communities and at different times, death from ingested poisons average about 25 per cent of the total.

Aside from the individual and social factors underlying suicide and homicide the most important point for consideration is the availability of poisonous materials. With the wide range of choice as indicated in the above list it is evident that the first three or four must be relatively easy to get hold of in poisonous amounts. It

[1] International List of Causes of Death, Nos. 163 and 175.

becomes necessary therefore to review briefly the open sources from which each poison is obtainable.

Arsenic.—Realgar (As_2S_2) is the red sulphide of arsenic, and orpiment (As_2S_3) the yellow amorphous trisulphide. The latter is used in low grade shellacs and in combination with quicklime as a depilatory by tanners.

Arsenic iodide (AsI_3) is a keratolytic used in the treatment of skin diseases and with the iodide of mercury in aqueous solution forms Liquor arseni et hydrargyri iodidi or Donovan's solution.

The arseniate of iron ($Fe_3As_2O_8$) is a medicinal tonic.

Arsenate of lead ($Pb_3(AsO_4)_2$) is an insecticide.

Scheele's green ($CuHAsO_3$), hydrocupric arsenite is widely employed in the form of a spray in gardens and orchards and as a pigment in wall paper and artificial flowers.

Paris green $(CuAs_2O_4)_3\ Cu(C_2H_3O_2)_2$, acetoarsenite of copper, is used to form a surface film on water in mosquito control.

Veterinary worm balls contain 1.3 per cent of arsenious acid, veterinary tonics 5 to 10 grains per dose.

Rat poison has 5 per cent arsenious acid and fly-water variable amounts of the same in a treacle or honey mixture. Fly-paper is an absorbent paper impregnated with arsenious acid.

Arsenical sheep dips contain about 1 per cent arsenious acid and arsenical soaps for preserving pelts as high as 20 per cent.

Many fireworks have from 2 to 6 parts of realgar, metallic arsenic or arsenious acid.

Arsenic trioxide (As_2O_3), arsenious acid, white arsenic, or arsenious anhydride is the form of arsenic most commonly employed in the arts and medicine. When arsenic is spoken of generally in the trades it is this form which is meant. It is marketed in amorphous cakes, in vitreous form, or as crystals. All forms are sparingly soluble in water. Taylor makes the general statement that 1 ounce of cold water dissolves 0.5 to 1 grain of arsenious acid.

The medicinal preparations of arsenic, either as official drugs or compound prescriptions, contain small amounts of arsenic trioxide or one of the other salts of arsenic. Fowler's solution (Liquor potassii arsenitis), Pearson's solution (Liquor sodii arsenitis N.F.), and Donovan's solution (Liquor arseni et hydrargyri iodidi) are all made up to the single dose of 1 to 5 minims (0.06 to 0.30 gram), while the solid forms as arseni trioxidum, arseni iodidum and sodii arsenas (B. P.) are given in single doses of $\frac{1}{10}$ to $\frac{1}{100}$ grain (0.006 to 0.0006 gram).

Although there are legal restrictions on the indiscriminate sale of arsenical preparations in the retail trade any one can purchase several pounds of white arsenic in the wholesale market. Farmers, nurserymen, hostlers and other traders can purchase orpiment or

arsenious acid for the purpose of making up sprays or veterinary medicines without restraint.

Druggists on the other hand cannot sell even small amounts without complying with regulations which require the keeping of a record of the name and address of the purchaser, the amount sold, and the alleged purposes for which it was bought. Most retail druggists will dispense arsenicals only on physician's prescriptions.

Arsenic is incorporated in various pastes, washes, fillers and pigments used in wall paper, wall paints and washes, wood preservatives and distempers. Its main purpose in these is as a deterrant *to cock-roaches, termites, wood-borers and other destructive insects,* and moulds.

Since many of these commercial preparations are available at supply houses an opening is left for the purchase of arsenic in one form or another by any one desiring it for suicidal or homicidal purposes. It is also readily available by removing it from any of the articles containing it such as matches, fly-water, fly-paper and wall-paper or pastes.

A poisonous dose of arsenic is generally considered as any amount over $\frac{1}{2}$ grain, a dangerous dose as 3 grains. The lethal dose is far from absolute. Deaths have been reported from as little as $2\frac{1}{2}$ grains.

Arsenic trioxide is tasteless and in small amounts has very little odor. It can readily be incorporated in powders, pastries and colored beverages without fear of detection except by chemical tests. Homicides have resorted to its use for slow poisoning in almost every common table food.

Attempts at suicide are frequently frustrated because of the vomiting induced by the relatively large amounts of irritating solutions which must be taken in order to get a lethal dose of the arsenic. It would take 300 or more cc. (10 ounces) of a liquid containing 1 per cent of arsenic trioxide to make sure that a dangerous amount was taken even if all of it was retained.

The rate and amount of absorption of arsenic is very irregular depending on the amount of food present, the solubility of the form of arsenic used and the amount eliminated by vomiting and diarrhea.

Under the most favorable conditions arsenic is absorbed very rapidly and enters the general circulation at once. It has a depressant effect on the heart and vasomotor mechanisms so that the blood-pressure falls and the pulse becomes weak and thready. Collapse may occur as a result of this depression possibly because the vessels of the abdominal viscera dilate as in shock and contain an abnormal amount of the total blood supply. Following lethal doses circulatory depression continues, the patient becomes exhausted from the profound metabolic changes and the constant

purging, the kidneys show a toxic nephritis severe enough in some cases to produce suppression of the urine, and death occurs in coma.

Smaller doses and cases of chronic poisoning exhibit any of the above symptoms in milder degree and show further evidences of damage to other structures. The skin becomes pale and pasty and frequently develops an eczematoid condition or breaks out in a papulopustular acneiform eruption. There is a strong tendency to upper respiratory catarrhal symptoms and irritation of the conjunctiva with a pseudo-jaundice discoloration of the eyes. Neurologic symptoms vary from a widespread neuritis with sensory or motor changes, or both, to muscular twitchings and spasm or generalized convulsions.

Arsenic is eliminated slowly through the kidneys but also by way of all other secretions. It may make its appearance in the stomach and intestines by passage through the walls of these organs long after the original dose has disappeared from within them.

Some arsenic is retained for long periods in the liver, muscles and bones from which it is gradually lost in cases which recover.

Hydrocyanic Acid and the Cyanids.—The chemical description and toxicology of these substances have been considered under Poisons Acquired by Inhalation, page 139.

Pure concentrated liquid hydrocyanic acid (Prussic acid) is one of the most highly poisonous substances known. This, in the popular sense means extremely rapid poisoning with death from very small amounts of the poison. Hydrocyanic acid in this form is kept only in laboratories and is therefore hardly available to the public except by theft.

Dilutions of the acid are sold by pharmacists in solutions of 5 per cent or less. Official acidum hydrocyanicum dilutum is 2 per cent. Sheel's acid is 4 to 5 per cent HCN. Druggists in this country are permitted by law to sell hydrocyanic acid in retail amounts provided they keep a record of the sale, but they generally dispense it only on prescription.

Potassium and sodium cyanid are common articles of commerce. They are used by engravers, gilders of silver and other metals, dye makers (Berlin blue and black silk dye), photographers, and miners who employ the cyanid method of ore extraction. The single salts of sodium, potassium, silver, gold and mercury are all poisonous. The double salts such as ferrocyanid of potassium are non-toxic.

Because of the widespread use of these cyanids in the trades there is no restriction on their sale in wholesale quantities.

Oil of bitter almonds contains about 10 per cent anhydrous prussic acid. Enough hydrocyanic acid can readily be obtained by the distillation of cherry laurel water to form a fatally poisonous drink.

Just as bitter almonds, wild cherry pits and peach kernels can cause death by accidental poisoning, so these same substances can be taken with suicidal intent.

Hydrocyanic acid content of HCN-bearing plant products:[1]
1 gram of bitter almond pulp = 2.5 mg., anhydrous HCN.
1 gram cherry stones = 1.7 mg. anhydrous HCN.
Service-tree bark = 0.02 per cent HCN.
Cherry laurel leaves = 0.39 per cent HCN.
Cassava root = 0.0168 per cent HCN.
Bitter cassava root = 0.0275 per cent HCN.
Peach kernel = 0.17 per cent HCN.
Plum stones = 0.056 per cent HCN.
Apple pips = 0.035 per cent HCN.

Prussic acid and its derivatives is the favorite medium for suicide by professional photographers, chemists and physicians. Its use by others has increased through the publicity given to this medium.

The accepted minimal lethal dose (Taylor) of commercial prussic acid is an amount equivalent to 0.065 gram (1 grain) of anhydrous acid; that of potassium cyanid 0.157 gram (2.4 grains).

Emerson[2] states that this same amount, on the average, would be obtained from 80 bitter almomds.

Opium and Its Derivatives.—For the poisonous effects of opium see Poisons Acquired by Inhalation: Opium page 171. Raw opium is so seldom seen in Western markets that it is hardly to be considered as a medium for suicide or homicide in occidental countries. Its preparations however stand at the top of the list of substances used with intent to kill.

The following list of medicinal preparations and their opium or morphine content is compiled from Emerson's monograph on poisons:
Powdered opium = 10 per cent anhydrous morphine.
Tincture of opium (Laudanum) = 1 per cent morphine.
Tinctura opii camphorata (Paregoric) = 5 mg. of morphine in 10 cc.
Compound powder of opium (B. P.) = 10 per cent opium.
Pill of lead and opium = 12 per cent opium.
Compound powder of kino = 5 per cent opium.
Aromatic powder of chalk and opium = 2.5 per cent opium.
Ipecac and opium powder (Dover's powder) = 10 per cent opium.
Dry extract of opium = 20 per cent morphine.
Liquid extract of opium = 0.75 per cent morphine.
Liniment of opium = 0.5 per cent morphine.
Compound soap-pill = 20 per cent opium.
Ipecac and morphine lozenges = 2 mg. morphine hydrochloride in each.
Morphine suppositories = 17 mg. morphine hydrochloride in each.
Solutions of morphine acetate and hydrochlorate.
1 part by weight of each in 100 parts by measure.

[1] Blythe, A., and Wand, M. W.. Poisons: Their Effects and Detection, London, C. Griffin & Co., Ltd., 1920.

[2] Emerson, R. L.: Legal Medicine and Toxicology, New York, D. Appleton & Co., 1909.

Solution of morphine tartrate = 1 part by weight in 100 parts by measure.

Godfrey's cordial = 1½ grains of opium to each fluidounce.

Ginrod's spasm remedy = 1 grain of morphine hydrochloride in each 6 ounces.

Nepenthe = 1 per cent meconate of morphine.

Black drop (acetum opii) = 4 per cent morphine.

Powell's balsam of aniseed = $\frac{1}{16}$ grain morphine in each ounce.

Dalby's carminative = 5 drops of laudanum in each 2 fluidounces.

Chlorodyne = 8 grains morphine hydrochloride in 10 drams.

Pantopium hydrochloride (Pantopon) is a preparation of the combined alkaloids of opium. Dose, ⅙ to ¼ grain.

The open sale of opiates is, in most countries, regulated by license and strict laws governing the amount which can be stocked and dispensed by dealers. With a few exceptions (paregoric in U. S.) they can only be sold on physician's prescriptions. The physician also is required to possess a special narcotic license. Both prescribers and dealers must keep a record of the amounts ordered and to whom sold. Allowances and exemptions are made which permit the sale without prescription of preparations containing not more than stated small amounts of opium or morphine.

The sale of opiates by manufacturing and wholesale druggists and chemists is likewise regulated by license and they may sell only to stipulated professional or commercial institutions or individuals.

Such regulations largely preclude the possibility of obtaining opiates through legitimate channels in large enough amounts for suicide or homicide. They leave the would-be suicides and homicides the necessity of accumulating sufficient quantities of the drug legitimately over a period of time, or resort to theft and subterfuge. In rural homes it is not uncommon to find relatively large amounts of laudanum, paregoric, opium pills and soothing syrups which have been so accumulated or bought in large amounts for veterinary purposes. The remoteness of these areas from immediate medical aid is the excuse given for keeping large quantities on hand.

In urban communities there are always illegitimate sources of narcotics for those who will seek them out.

The amount of opium or morphine which may prove fatal in a single dose varies with the age of the individual, stage of digestion, and form in which it is taken. Children tolerate it poorly and death may result from the ingestion of as little as $\frac{1}{20}$ grain. For adults anything over 4 grains (0.26 gram) of opium, 2 drams (8.0 cc.) of laudanum, or 3 grains (0.20 gram) of morphine may cause death.

Mercury.—Mercuric chloride has long been used as a suicidal and homicidal poison. It is a common ingredient of antiseptic tablets and powders and as such is one of the most available of all of the metallic poisons. Its common commercial name is corrosive

sublimate and in medicine it is known most generally as bichloride of mercury (Hydrargyri chloridum corrosivum U. S. P., Hydrargyri perchloridum, B. P.) "Bichloride poisoning" always means mercury.

In the markets, bichloride of mercury is sold in transparent, *colorless masses or the powder made from them. It is soluble in* 16 parts of cold and 3 parts of boiling water. The routine dilution for antiseptic uses is 1 to 1000 and it may be purchased in this form or as tablets containing 0.5 gram (8.0 grains) each of the salt, one of which when added to 500 cc. (1 pint) of water forms this dilution. Most of the suicides employ these concentrated tablets or a solution of them. (Bichloride of mercury tablets for surgical use are official as Toxitabellæ hydrargyri chloridi corrosivi, U. S. P.). Alkalies and sodium chloride enhance its solubility. It is soluble in 3 parts of alcohol.

Metallic mercury in the finely divided state is used in the blue pill (Pilula hydrargyri), liniment of mercury (Linimentum hydrargyri) and mercury and chalk powder (Pulvis hydrargyrum cum cretæ). Each of these may be taken internally as poisons. The blue pill and chalk powder each contain 33 per cent and the liniment 9 per cent of mercury.

Cyanid of mercury produces poisoning through the action of the mercury radicle and not the cyanid. Calomel or mild mercurous chloride (Hydrargyri chloridum mite) has wide popularity as a purge and is given in doses ranging from one to 20 grains.

There is no advantage in the larger doses because only a small part of it is absorbable by being changed to the gray oxide and the remainder is excess waste. Large doses in children may produce toxic effects through this absorbable quantum of the dose. The mild chloride may be converted into the corrosive chloride.

The iodides of mercury are toxic in large doses but seldom resorted to for criminal use.

Due to the almost unlimited use of the double chloride of mercury as the salt of choice in deliberate mercurial poisoning the following discussion will apply to it.

Mercury ingested in toxic amounts exerts its first effect as a corrosive coagulant of the mucous membranes. If left for any time in *concentrated form in contact with living mucosa it enters into combination* with the proteins and forms albuminate of mercury. Local death of the affected tissue is evidenced by the necrotic eschar on the lips and in the mouth of a patient who has taken a concentrated solution of bichloride. This corrosive effect continues as far down the alimentary tract as the amount and concentration of the poison permits it to act before dilution or combination with albuminoids renders it innocuous.

The corrosive effect is itself serious by interfering with swallowing and therefore nutrition. Subsequent scarring and constriction may

result in a person who has not otherwise suffered greatly from absorption of mercury.

For the general effects of mercury and the symptoms of chronic poisoning the reader is referred to the section on Poisons Acquired by Inhalation; Mercury, page 155.

The lethal dose of bichloride of mercury is generally placed at 3 to 5 grains (0.2 to 0.3 gram) but many other factors must be considered such as concentration, local corrosive effects and solubility of the preparation. A single antiseptic tablet in a glass of water may produce death if it is not lost by vomiting or overcome by treatment.

The bichloride of mercury and other salts of this metal can be administered in smaller doses over a period of time and thus produce a serious or fatal subacute or chronic form of poisoning. The crude powders and solutions have a disagreeable metallic taste making them difficult to disguise in foods or beverages. The gastrointestinal symptoms in these cases is not due to the primary corrosive effect of the drug but to its continued elimination through the walls of the alimentary tract and in the saliva. Salivation, mercurial stomatitis and tremors are the outstanding clues on which mercury poisoning may be suspicioned.

Phosphorus.—In the days of the old "strike-anywhere" matches, phosphorus was the poor man's poison. Phosphorus tipped matches were available anywhere and it was a simple process to soak off the heads and make a poisonous concoction of them. The average content of a match head was about 75 per cent yellow phosphorus. One hundred English match heads yielded an average of 32 mg. of phosphorus. Phosphorus sesqui-sulphide and red amorphous phosphorus have replaced yellow phosphorus almost completely in modern matches and greatly reduced the possibilities of poisoning from this source.

Vermin pastes containing phosphorus are still in use. They are made up of phosphorus, 1 to 2 per cent in combination with flour and sugar and some binding oil or butter. The only official medicinal preparations of phosphorus are Pilulæ phosphori, dose $\frac{1}{100}$ to $\frac{1}{50}$ grain (0.0006 to 0.0012 gram) of phosphorus; Oleum phosphoratum, dose 1 to 5 minims (0.05 to 0.3 gram); Spiritus phosphori, dose 1 to 5 minims (0.05 to 0.03 gram); Elixir phosphori, dose 15 minims to 1 dram (1 to 4 grams). The dose of $\frac{1}{20}$ grain of phosphorus is a dangerous maximum therapeutic limit.

The lethal dose of phosphorus as judged by the amounts allegedly consumed by fatal cases probably averages around 1 to 2 grains (0.06 to 0.12 gram). Emerson states that the ends of two phosphorus matches have proven fatal to children.

Phosphorus acts as a cellular poison, producing an irreversible degeneration in the cells of many organs, especially the liver. Its

effect on this latter organ gives all of the clinical picture of acute yellow atrophy of the liver.

The local gastro-intestinal symptoms may set in within one-half to one hour after the ingestion of phosphorus or as late as eight to twelve hours after. The abdominal pain shows no peculiar characteristic. There may be vomiting and diarrhea, each showing a tendency to become bloody. Constipation is common after the subsidence of the original irritative effect. This may initiate a period of calm which is liable to be misinterpreted as improvement whereas the destruction in the parenchymatous organs continues.

In severe poisoning the patient may succumb before the onset of the more typical manifestations such as jaundice and clay-colored stools. The urine shows sarcolactic acid, due to the damage to muscle cells.

Death results from the widespread degeneration of such important structures as liver parenchyma, renal tubules, gastro-intestinal mucosa, pancreas cells and muscles. It may occur anywhere from the second to the eighth day in acute poisoning.

In chronic poisoning there is frequently involvement of bone. This is described more particularly in the section on Poisons Acquired by Inhalation: Phosphorus, page 161.

Strychnine.—The most readily available compounds containing this powerful alkaloid are common drugs found in the medicine cabinets of most homes. They are the familiar nux vomica tonics and some of the laxative pills. They can be purchased at any pharmacists in reasonable amounts and any one desiring to accumulate sufficient of them for suicidal reasons is presented with no obstacle against his doing so. In these forms however, strychnine could hardly be administered in sufficient amounts for homicidal purposes.

Strychnine is an alkaloid obtained from the seeds and bark of a flowering plant, *Strychnos nux vomica* or *Strychnos ignatii*. The seeds may be purchased in the market as well as a powder made from them which resembles licorice.

All preparations of strychnine are exceedingly bitter and it has been argued that the taste precludes their use for homicide. Incorporation in bitter foods and drinks disguises the taste sufficiently for a victim to take poisonous amounts before becoming aware of it.

Powdered strychnine is generally strychnine sulphate but may be the nitrate or hydrochloride. They are equally toxic and are administered therapeutically in doses of $\frac{1}{60}$ to $\frac{1}{20}$ grain (0.001 to 0.003 gram).

Official pharmacopœal preparations are Extract of nux vomica, Fluidextract of nux vomica, and Tincture of nux vomica. As has been stated above strychnine or nux vomica is a constituent of many proprietary and patent medicines used as general tonics,

stomachics and laxatives. The amount of strychnine is small in each recommended dose so that large amounts of the preparations would have to be taken to produce fatal results. This is not beyond possibility however.

The lethal dose of strychnine alkaloid for an adult probably ranges from 1.2 to 2 grains (0.03 to 0.12 gram). A relatively smaller amount is required in the case of children.

Because powdered nux vomica is now rarely employed for any purpose and the poisonings from it leave great doubt as to the amount which was used it is difficult to estimate its lethal dose. Three to 30 grains are the ranges in reliably observed fatal cases.

Strychnine powders are used by veterinarians and farmers to kill suffering and undesirable animals. It was formerly in vogue in rat pastes but this has been legislated out of existence as a commercial practice.

Strychnine in moderate doses stimulates the motor tract of the spinal cord and the nerve trunks and in poisonous doses depresses the motor nerve plates in the muscles.

The onset of symptoms after ingestion of strychnine are rarely delayed beyond one hour but may not occur until two or six hours later. The first evidences of poisoning may occur with explosive effects in an individual who was feeling perfectly well. The onset in such cases is a sudden convulsive stiffening of the body which takes place with such force as to throw the victim to the floor. More commonly there is antecedent stiffness of the neck or back muscles and the generalized spasm does not take place until the patient has complained and lain down.

The whole picture of strychnine poisoning is one of extreme irritability of the motor nerve mechanism so that it responds to the slightest stimuli. This effect continues until gradual exhaustion terminates in death.

A dangerous and possibly fatal single adult dose of strychnine would be acquired by taking the various preparations of strychnine in the amounts shown in the following table:

Strychnine sulphate, nitrate, valerate or hydrochloride tablets grains $\frac{1}{16}$ each, 24 tablets.
Extract of Nux Vomica, 15 grains (1 gram).
Tincture of Nux Vomica, 1 3 ounces (40 grams).
Fluidextract of Nux Vomica, 50 minims (3.3 grams).
Elixir of Phosphorus and Nux Vomica, 20 ounces.
Aloin, Belladonna and Strychnine Pills, 160 pills.
Alophen pills, 100 pills.

Chloral and the Barbiturates.—With increasing knowledge of their deep hypnotic effects and the danger of overdoses it is not unreasonable that these drugs should be resorted to as an easy form of death. The number of tablets or pills required precludes to a great

extent the possibility of their use for murder and leaves them largely for suicidal purposes.

The lethal amounts, aside from any question of idiosyncrasy, vary widely in this group.

The average dangerous doses are:

Chloral hydrate, 30 to 60 grams or 6 to 12 tablets.
Sulphonal, 50 to 80 grains or 10 to 16 tablets.
Barbital, 50 to 120 grains or 10 to 24 tablets.
Phenobarbital (Luminal), 25 grains.
For toxic effects see Drug Addiction, page 225.

The Corrosive and Caustic Poisons:

Sulphuric Acid (Oil of vitriol).
Hydrochloric Acid (Muriatic acid).
Nitric Acid (Aqua fortis).
Nitro-hydrochloric Acid (*Aqua regia*).
Carbolic Acid (Phenol) and derivatives.
Oxalic Acid (Acid of sugar).
Acetic Acid (Acid of vinegar).
Sodium Hydroxide (Caustic soda, lye).
Potassium Hydroxide (Caustic potash).
Ammonia and ammoniacal salts.
Iodine.

These substances are for the most part suicidal poisons selected by expediency rather than from choice. In some, such as carbolic acid, there is frequently some conscious selection because the user has heard or read of its successful use by someone else. Lack of knowledge of the agonizing pain and distress which they bring on seems to be the only reason why they should ever be taken through choice. The desperate suicide however will use anything which he knows to be effective for his purpose and only too frequently finds one of this group conveniently at hand.

The members of this group possess the characteristic in common of being immediate necrotizing agents to living tissue. When they are brought in contact in concentrated form with the living cells of the upper alimentary tract they cause the death of these cells by actual disintegration or coagulation. The difference in the appearance of the necrosed areas produced by the different poisons is due to changes occurring in the agent itself or products of its reaction with the constituents of the cells (*e. g.*, yellow xanthoprotein by nitric acid) or by the amount of carbonization, albumen coagulation, dissolution and solution of cells or changes in tissue and blood pigments.

In some instances (carbolic acid) there may be little gross evidence of pathology but examination reveals the living cells to be completely fixed and devitalized. The erosion may reach to or through the mucosa and result in denudation of the epithelium and

in severe cases may burn its way entirely through the walls of a hollow viscus such as the stomach and cause perforation. Whole casts of the esophagus have been vomited up after sulphuric acid burns.

Swelling and edema of nearby tissues can result either from direct contact with the corrosive which has become diluted or by its fumes. The most rapid deaths take place in those instances where some of the material has gained entrance to the respiratory tract. Closure of the glottis by swelling or edema of the lungs brings on rapid suffocation and death.

In most cases the contact of the material with the mouth and throat gives excruciating pain and muscle spasm. The intense burning can be felt the length of the esophagus and in the stomach when the fluid reaches that organ. Vomiting may be immediate or delayed and frequently contains shreds of dead discolored membrane and often blood. Diarrhea occurs later and the movements too become bloody.

If death does not occur very soon from suffocation and shock it may be delayed several hours and result from side effects due to the massive destruction of tissue and absorption of poison. When the general disturbance has not been severe enough to cause death a fatal outcome may result from interference with nutrition by destruction of essential mucous membranes and absorption of toxic products. Sequelæ, such as stenoses of the pharynx, esophagus, stomach, larynx or trachea may bring about death weeks or months after the injury.

Some of the corrosives and caustics produce special characteristic features by which poisoning by them can be recognized. These are indicated in the following consideration of the individual agents.

Carbolic Acid.—This strong organic acid is found in crystalline form or in solution. The former is rare outside of pharmacies, laboratories and institutions where it is kept in bulk. From it are made the weaker dilutions which are so widely used for disinfection. Commercial preparations, such as lysol and cresol are common phenol-containing antiseptics used for disinfection of articles which have been contaminated by discharges. They are also medicinal antiseptics used as douches and washes. Lysol is a mixture of cresols with sodium hydroxide. The popularity of phenol preparations makes them a common household article. This accounts in great part for their frequent use for suicide.

The minimum lethal dose of solid carbolic acid is generally accepted as about 15 grams (230 grains). A minute amount entering the glottis however may cause immediate death.

Carbolic acid solutions are usually fatal in amounts over 1 ounce (30 cc.) but this too is arbitrary.

Tissues burned with carbolic acid are literally cooked and give a characteristic white opaque layer of necrotic material. The typical white eschar on the lips and in the mouth, combined with the familiar antiseptic odor of phenol should point clearly to the poison taken.

Sulphuric Acid.—Oil of vitriol is one of the most common acids of commerce. It is employed in the manufacture of most other acids, in the production of glucose and in many other technical processes. On the market it exists as an almost colorless oily liquid 100 per cent pure acid or in cheaper grades of gradually darkening colors, through amber to dark red-brown. The dilute sulphuric acid of the pharmacopœia (Acidum sulphuricum dilutum) is 10 per cent strength. Sulphuric acid is also official as Acidum sulphuricum aromaticum in which it is combined with tincture of ginger and oil of cinnamon.

Suicide is generally the result of drinking the strong or weaker forms of the commercial acid.

Sulphuric acid is strongly escharotic and burns the tissues to an oily black carbonized mass. It is the corrosive mostly responsible *for the severe destructive burns which result in perforation of the* stomach.

Death may result immediately from inhalation of the acid or from shock. Delayed deaths result from altered nutrition or the absorption of soluble sulphates and their effect upon the kidneys. Stenoses are common if recovery from the immediate damage takes place. Cicatricial contraction of the orifices of Stenson's ducts frequently follows the healing processes and causes obstruction to the flow of saliva from the parotid glands.

No accurate statements can be made as to the lethal dose because of the many factors involved in its action. Sixty grains of the solid acid may cause death or as little as 2 drops of the concentrated liquid if it enters the glottis. If the stomach is empty and all of the material is swallowed, any amount over an ounce would very probably prove fatal.

Nitric Acid.—The nitric acid of commerce is either pure and almost colorless or impure and of colors ranging from yellow to red. Dyer's acid is 58 per cent HNO_3 and engraver's acid 70 per cent. Beside being used in these two trades it enters into the manufacture of sulphuric acid, gun-cotton, nitroglycerin and picric acid. It is also employed in making felt hats. It is found in all chemical laboratories and is used frequently around the home and workshop for cleaning metals and soldering.

It is official as Acidum nitricum and Acidum nitricum dilutum. The latter is 10 per cent strength.

Nitric acid is somewhat less corrosive than sulphuric acid but nevertheless produces widespread necrosis when taken in concen-

trated form and an intense inflammatory reaction when diluted. Devitalized tissue takes on a lemon yellow color which is characteristic of this poisoning.

This acid frequently causes delayed death due to the profound disturbance produced by its destruction of the gastric secretory tubules. Absorption of large amounts may cause serious damage to the renal epithelium through which it is eliminated. Blood may appear in the urine.

A fatal dose, excepting those instances in which death results from suffocation, must probably exceed 2 drams which is the smallest lethal amount recorded.

Hydrochloric Acid.—Commercial muriatic acid or spirit of salt finds its greatest use in the manufacture of chlorine. In the trades it is a common metal cleaner and ingredient of soldering fluids. It is therefore always available to any buyer and is on almost every work bench where metalcraft is carried on. Acidum hydrochloricum dilutum is 10 per cent strength.

The action of hydrochloric acid is almost identical in all particulars with that of nitric acid to which the reader is referred. The important exception is the color of the eschar which in the case of hydrochloric acid is brown.

The fatal dose, when taken without respiratory complications is probably ½ ounce or more.

Oxalic Acid.—This acid may be said to be the most common household poison used for suicide. It is a common ingredient of many cleansing powders and stain removers. Ink eradicators and iron rust removers usually have oxalic acid as their important base.

In the trades it has much the same uses but extended to a broader application, such as a metal cleaner, textile and straw bleacher and leather finisher. The bioxalate (Hydropotassic oxalate, "essential salt of lemon," salts of sorrel) is used for the same purposes and possesses the same and almost equal toxic effects as oxalic acid. (Because oxalate crystals are not readily distinguished on casual examination from magnesium sulphate (Epsom salts) accidental poisoning from this mistake has been reported.)

Almost all suicides from oxalic acid have resulted from swallowing it in crystalline form or concentrated home-made solution. It produces an intense sour taste followed immediately by burning. This latter can be felt in the esophagus and stomach as the acid is swallowed. In most cases it produces almost immediate vomiting which soon turns brown or black due to altered blood.

Death from a heavy dose may occur in a very few minutes due to shock and the corrosive effect. If it is delayed beyond ten or twenty minutes the absorbed oxalate produces marked suppression of the pulse, collapse, muscle cramps and twitching, convulsions, numbness and eventual cardiac failure and death.

Christison,[1] in his classical description says that "if a person immediately after swallowing a solution of a crystalline salt, which tasted purely and strongly acid, is attacked with a burning in the throat, then with a burning in the stomach, vomiting, particularly of bloody matter, imperceptible pulse and excessive languor and dies in one-half hour, or still more frequently in twenty, fifteen or ten minutes, I do not know any fallacy which can interfere with the conclusion that oxalic acid was the cause of death."

Taylor records the smallest fatal dose as 60 grains but larger doses have been recovered from. One-half ounce of the crystals will usually cause death.

Sodium Hydroxide and Potassium Hydroxide.—The fixed alkalies are common accidental poisons but are rarely used for suicide. In the home and in the trades they are used in cleaning and scouring powders and as fat and oil cutters and renderers. Most of the drain pipe openers contain lye. Potassium hydroxide is also an ingredient of horn softeners and some manicure solutions.

The caustic alkalies do not carbonize the tissues as do the corrosive acids but produce a gelatinous coagulation and solution of the cellular tissues. This results in swelling, denudation and hemorrhage. The swallowing of caustics is attended by an intense burning and vomiting, the latter usually black from altered blood.

Death occurs from shock and severe alkalosis or may be delayed for days or months from secondary stenosis and contractions.

Ammonia.—Ammonia taken for suicidal purposes is generally taken as a drink of its aqueous solution or in the form of its common salt, ammonium carbonate. Liquid ammonia is ammonium hydroxide. The common fluid found in the household for bleaching, washing and blueing is a solution of ammonium carbonate.

Ammonia and its salts acts as a caustic alkali and produces the same effects but in addition the liberated ammonia gas frequently enters the respiratory tract and causes intense irritation and even suffocation.

Death may result from suffocation, collapse, a severe gastro-enteritis or the latent effects from destructive lesions. No accurate estimates can be made as to its fatal dose.

Iodine.—Attempts at suicide by drinking tincture of iodine are frequent but rarely fatal. It has recently become the poison of choice by young women in distress but fortunately the gesture is most often without fatal results.

Iodine produces an intense burn of the mouth, esophagus and stomach and sets up a severe gastro-enteritis. Vomiting is early and frequent and most of the material is lost in this way before

[1] Christison, R.: Treatise on Poisons. Second edition, p. 207. Adam and Charles Black, Edinburgh, 1836.

much damage is done. It is quickly diluted and rendered inert by the secretions.

If iodine enters the trachea choking ensues which may conceivably be fatal very soon or later as the result of edema and secondary pneumonia.

Chloroform.—When chloroform is taken internally it produces a deep anesthesia similar in all respects to that seen after its inhalation. It acts first as a local gastric irritant. For some reason there is a considerable delay in the development of its general anesthetic effects and death may not occur for several hours from cardio-respiratory failure.

Two ounces or more would seem to be needed to produce death in an adult.

Methanol (Wood Alcohol).—This alcohol, in amounts over 1 ounce, may cause death by respiratory paralysis. The terminal coma is preceded by giddiness, headache, blurring of vision or sudden blindness, incoordination and delirium.

Wood alcohol is, or was formerly, a familiar household article used for many purposes such as cutting paints and varnishes, as a fuel in spirit lamps and as a cleansing fluid and spot remover. It is now almost wholly replaced by newer and more efficient chemicals. It is found occasionally in cheap whiskies and as such may be used for poisoning. As it is a basis of shellac it may be taken for suicidal purposes in that form. Attempts at suicide have been reported by drinking cologne spirits and bay rum which contain wood alcohol.

Turpentine.—Turpentine is a common solvent vehicle in paints and varnishes and is also employed to clean old paint off of furniture, etc. It has caused death in suicides but rarely has been used for homicide.

Swallowing of turpentine is followed by painful burning in the mouth and throat, vomiting and diarrhea. It is eliminated in the urine and its passage through the kidneys frequently produces sufficient irritation of the renal and lower urinary epithelium to cause hematuria. The urine possesses a violet-like odor.

Kerosene.—Kerosene is used as a fuel and cleaning fluid. It is always purchasable in large quantities and is used by the poorer classes in cities because of its cheapness and on the farm because of the absence or expense of other fuels.

The ingestion of kerosene in lethal amounts causes vomiting and collapse and eventual death from circulatory failure. The latter may be deferred for several hours and take place suddenly without warning.

Conium or Hemlock.—The active toxic principle of poison or spotted hemlock (*Conium maculatum*) is conine. This is a paralyzant alkaloid which acts primarily as a depressant to the motor

nerve trunks. Poisoning from hemlock produces most frequently an ascending paralysis which in fatal doses eventually involves the nerves of the muscles of respiration. Coma and convulsions may precede the final paralysis in some cases.

Conine is found in all parts of the hemlock plant. As a medicine it is used as Extractum conii, Tinctura conii, Succus conii (B. P.). A dangerous dose of the solid extract would well exceed 1 grain and more than 1 or 2 fluidrams of the liquid preparations would be necessary to produce serious poisoning.

Conium is rarely prescribed and its use for criminal purposes or self-destruction is largely one of historical interest.

Aconite.—Aconite is one of the most powerful poisons known. It is obtained by extraction from *Aconitum napellus*, a flowering shrub commonly grown in gardens for ornament and known as Monkshood or Wolfsbane.

Its active alkaloid is aconitine, a paralyzant in toxic doses of the motor tract of the spinal cord and peripheral motor nerves and in fatal doses a depressant of the respiratory center to the point of complete paralysis.

Taken internally aconite causes a tingling sensation on the lips and in the mouth. This increases to a hot, burning intensity. The pulse is slowed by its stimulating action on the vagus nerve as soon as absorption from the stomach has taken place. Excessive dosage ultimately causes the pulse to become running and rapid.

The pharmaceutical preparations of aconite are Tinctura aconiti (0.04 per cent aconitine). Extractum aconiti, Fluidextractum aconiti and Linimentum aconiti (B. P.).

Aconitine is given medicinally in the dose of $\frac{1}{400}$ to $\frac{1}{200}$ of a grain (0.00015 to 0.0003 gram). As little as $\frac{1}{10}$ grain (0.0065 gram) may prove fatal to man.

Any amount of the tincture over 15 minims is likely to prove exceedingly dangerous. Of the root of the plant itself, 60 grains have caused death.

Physostigmine.—Physostigmine is the alkaloid found in the seed of the Calabar bean, *Physostigma venenosum* or ordeal bean. This alkaloid, also called eserine, produces death by respiratory paralysis. Convulsions may occur if a second alkaloid of the bean, calabarine, be present.

The sensory cord is involved but the sensory nerves are not affected. A partial depression of the motor nerves results in incoordination and muscular twitching, which in fatal cases goes on to paralysis.

Extractum physostigmatis (B. P.) and eserine salicylate are official preparations. Blythe states that 3 grains (0.2 gram) of physostigmine would be much beyond the fatal dose.

DEFENSE AGAINST THE USE OF SUICIDAL AND HOMICIDAL POISONS.

The logical defense against suicide and homicide is directed against the social and behavioristic factors which engender the motives for the act.

The main aspect of the defense against the willful use of these poisons must involve a study of methods which will be effective in placing obstacles in the path of the would-be murderer or suicide who is desirous of obtaining them in lethal amounts.

The ineffectiveness of such an effort in general must be admitted at the outset because of the ready availability of fatal poisons to any one who seriously contemplates death to others or himself. Of the potentially fatal poisons listed the majority can be obtained with little effort and without subterfuge. As previously stated the homicidal criminal and suicide may find it difficult to obtain his poison of choice. This is especially true of the poisons most commonly used, such as the opiates. This apparent contradiction is explained by the fact that those who have accessibility to these poisons use them while those who do not, use methods other than poisoning. Physicians, druggists and chemists for example use those poisons most difficult to be obtained by the non-professional man, the ignorant use the corrosive and caustic poisons, the majority of suicides and homicides use firearms or cutting weapons. Anti-narcotic and Poisons Acts are effective in blanketing the hurried suicide and non-contemplative murderer from purchase and possession of poisonous substances falling within the meaning of these acts. To obtain these poisons in lethal doses involves planning and cunning which does not characterize the impatient criminal or suicide.

Physicians in general prescribe poisonous drugs in excess of the amounts needed for the immediate treatment of their patients. The surplus is seldom thrown away but allowed to stand for long periods in medicine chests and on open shelves. These then constitute sources of poisons for deliberate use and those made up in alcoholic menstra remain not only poisonous in the original amounts but become more so because of the slow evaporation which increases the concentration of their poisonous ingredients.

Many of the poisonous proprietary medicines should be legislated out of existence not only because they are poisonous but because they are unnecessary and dangerous for self-medication. Every effort which the physician can make to rid the public of this menace through individual or concerted effort will aid in reducing the availability of lethal poisons.

Education remains as the one great measure against the misuse of toxic substances. The public should know that many household articles are potential suicidal and homicidal instruments. It should

be educated to suspect the development of suicidal tendencies in individuals who develop morose and melancholic behavior and to anticipate antisocial acts on the part of others who are entering the paranoid states with persecutory delusions. It is not implied that they can be expected to diagnose mental diseases but they can be taught to recognize poor mental hygiene and encourage medical consultation for those who appear mentally and emotionally sick.

"Poison" labels are required by law on many articles of commerce containing poisonous ingredients. This is primarily to reduce accidental poisoning but it is also useful as a warning not to allow them to stand around in places where they can be gotten hold of by irresponsible persons.

The widespread use of arsenic, cyanids, and mercury salts in the trades and industries makes it impossible to restrict their sale without interfering seriously in their legitimate use. The best that can be done at present is to make them difficult to purchase by unknown or unauthorized individuals and whenever this is impractical to make it mandatory for the dispensers to keep a complete record of the sale.

INGESTED POISONS ACQUIRED IN THE INDUSTRIES.

Almost all of the poisons acquired by accidental ingestion in the industries are the ores or salts of the heavy metals or the metals themselves.

In the extractive processes in which ores are ground and treated the workers may be subjected to contamination of their hands by finely divided particles and dusts which are readily carried to the mouth. Even though no visible dust may be apparent in the atmosphere these minute fractions of the minerals may rub off and contaminate the person or his clothing. This exposure differs in many ways from the inhalation of volatilized minerals or their dusts and is therefore given this special consideration under ingested poisons. In the intermediate and advanced stages of manufacture of many articles of commerce there are further possibilities for the transfer of these poisonous substances to the mouth.

Antimony.—This metal is used to increase the hardness of lead in printer's type and in the form of antimony sulphide enters into the manufacture of red rubber.

No convincing evidence has been brought forward to prove that the alleged cases of antimony poisoning in type-metal makers and printers are due entirely to antimony and not to the lead or arsenic impurities in the metals.

Investigations on the solubility of antimony sulphide in human gastric juice by Carlson[1] showed that 8 per cent of the crimson and 3 per cent of the golden sulphide mixtures went into solution.

[1] U. S. Bureau of Labor Statistics, Bull. 179.

The heavy contamination of the hands of workers in the type and rubber industries makes it highly probable that sufficient antimony may be carried to the mouth to account for the ingestion of considerable quantities of this metal. Further opinion of the rôle it plays in industrial poisoning must await the separation of its toxic effects from those of its associated elements.

Arsenic.—The prevalence of arsenic dermatitis in workers who handle arsenic-containing powders is evidence of the degree of contamination that exists in these industries. Although the great majority of occupational arsenic poisonings are due to the inhalation of dust and fumes there can be little doubt that there is an added hazard from its accidental ingestion.

For a list of the trades and industries in which arsenic is in use the reader is referred to page 266.

The toxic effects are discussed under Poisons Acquired by Inhalation: Arsenic, page 149.

Barium.—The insoluble barium salts except barium sulphate may be converted into soluble toxic barium chloride through the action of the hydrochloric acid of the stomach thus making them potentially poisonous. Barium salts are manufactured in large quantities for their use in medicine, especially as opaque media for roentgenography.

They are also used in paints and rat pastes. Barium nitrate and chlorate are ingredients of pyrotechnics and the carbonate and oxide are used in the manufacture of glass. Barium sulphide is a depilatory employed by dealers in hides and is a constituent of cosmetic hair-removers.

Poisoning by ingestion of barium salts in industries is rare not because of the lack of opportunity for it to reach the mouth but because large amounts are required to produce toxic effects. Chronic poisoning is said to produce whitening and loss of hair, vague gastro-intestinal symptoms and disturbance of the heart rate, muscular twitching and paralysis. In fatal doses it acts much like digitalis in its effect on the heart.

Cadmium.—Zinc ore contains a small amount of cadmium as an impurity which is liberated in the zinc smelting process. Tracinski says that small repeated doses may produce poisoning. This is acquired largely by inhalation of cadmium fumes but the possibility of ingesting small amounts over a long period of time must be kept in mind.

Lead.—The toxicology and industrial aspects of poisoning from this element have been fully discussed under poisoning from volatilized lead (page 157). Workers with lead cannot avoid getting it on their hands and under their nails. Unclean habits and failure to wash the hands before eating make it possible for considerable amounts of lead to be carried to the mouth in this way.

Much, if not most of the lead inspired with air is swallowed and therefore indirectly ingested. The rôle of directly ingested lead is probably a minor one in contrast to the other channels of entry. Hamilton states that painters are the lead workers who are not ordinarily exposed to lead dust but they too rub up dry lead powders.

Phosphorus.—The use of poisonous white phosphorus in the match industry was formerly associated with the development of many cases of phosphorus poisoning.

Although it is the inspired fumes of phosphorus which are especially dangerous it may be carried to the mouth on chewing tobacco, chewing gum, drinking utensils and tooth picks.

The processes and symptoms of poisoning from phosphorus acquired by ingestion are the same as those following its inhalation (see page 161).

PREVENTION OF THE INGESTION OF POISONS IN INDUSTRY.

With few exceptions the prevention of such poisoning rests almost entirely on the hygiene of the worker. Even though the employer may be negligent in protecting his workers by anti-dust measures the man exposed to harmful dusts must protect his own welfare by the adoption of hygienic habits. If it is granted that he knows there is danger in the dust it is grossly careless of him to place dirty fingers in his mouth or to handle anything he is going to put in his mouth with dirty hands. The responsibility of informing him of the danger involved in his occupation must rest on the employer. Reminders in the form of placards and danger signs would perform a real service.

The independent worker, such as a painter, is almost always aware, *through hearsay, of the dangers of lead poisoning. With him cleanli*ness means safety.

Legislation and agreements between employee organizations and *employers play an important part in insuring healthy working* conditions which will limit the possibilities of getting poisonous substances into the mouth.

In the larger industries the industrial physician is charged with the responsibility of protecting the health of the worker and it is he who must instruct the men and make health recommendations to the employers.

CHAPTER XXI.

POISONS ACQUIRED BY THE SKIN AND OTHER PARENTERAL TISSUES.

When chemical agents come in contact with the skin or other parenteral tissues and produce disease they do so by: (1) entering into chemical changes with the tissue cells; (2) initiating reactionary changes of an allergic nature in tissues sensitized to them; (3) passage through the tissues with the production of toxic effects on structures more or less remote from the tissue of entry. Under special circumstances the toxic agent may be introduced through the skin or other tissues without coming in contact with them. In such instances the poison may act on distant cells after it is absorbed or may secondarily involve the tissue through which it was introduced. This is seen in poisons acquired by deep inoculation.

Parenteral tissues include all relatively superficial membranes other than those of the gastro-intestinal tract. (The respiratory system is a parenteral system but poisons acquired through it have been considered elsewhere.) Those included in this category are the skin and its extensions, the nose, conjunctiva, auditory canal, urinary tract, genital tract, and the rectum. The latter is placed arbitrarily in this group because the discussion of poisons introduced into the alimentary tract has been limited to those acquired by ingestion. The processes of poisoning by substances introduced by rectum and their prevention are distinct from those taken by mouth.

The natural history of poisons acquired through these channels extends into the environment: it includes the sources from which they arise, the mechanisms by which they are brought into contact with the organism, and the disease changes which they bring about. (Pathologic lesions in the skin and other parenteral tissues which result from poisons acquired through other atria do not fall within this classification. Thus the eruption caused by the ingestion of bromides, or tumors of the bladder arising in poisoning from the inhalation of anilin are not primary effects.)

SOURCES AND METHODS OF ACQUISITION.

The human environment contains hundreds of potential contact poisons and their number is increasing with the technologic advances in processing and fabrication of the most common articles of daily

use. An outline of the preventive possibilities against these substances must first consider their origin and nature.

Numerically, the greater part of the skin poisons arise in industrial processes and their effects constitute the occupational dermatoses. The worker with crude products is brought into contact with ores, metals, acids, alkalies and salts which may in no way affect the users of the completed product. On the other hand the user may be poisoned by the materials of the finished article and the manufacturer remain completely unaffected. From these two main sources arise the majority of poisons that primarily affect the skin.

A third group includes crude chemicals and other substances of a relatively primitive nature which are ingredients of domestic supplies. These are represented by lye, washing soaps and scouring powders, disinfectants, deodorants, vermin deterrents, lacquers, varnishes, polishes and cleaning fluids.

Certain substances are deliberately used upon the person and are capable of causing damage. They are found in face powders and creams, wart and freckle removers, softeners for corns and callouses, eye washes, eyelash and hair dyes, medicated ointments, liniments and pastes, depilatories, manicuring preparations, and deodorizing powders and solutions.

Chemical poisons may be introduced accidentally into the eye, nose and ear, or may be deliberately placed there for therapeutic purposes. In the same way various harmful substances may be employed in the vagina, urethra, bladder, and in exceptional circumstances, the upper urinary tract. The use of venereal disease preventives and contraceptives may not always be without danger.

There are a number of plant poisons such as poison ivy, poison oak and sumac which can produce severe dermal reactions in susceptible individuals. A few woods (box-wood, red-wood, teak) also possess irritating properties. Such poisons are met with in their natural state or in manufacturing processes in which they are handled.

Some animal products such as dander, hair and poisonous secretions and excretions are skin irritants. These are acquired from pets, domestic animals, furs and fur products, hides, pelts, hair goods, bristles, and rarely from animal products used as foods. Fishermen, sportsmen, and collectors may be exposed to these poisons, and others may come in contact with them under a variety of circumstances.

Of the poisons introduced by inoculation, the most common are those of stinging and biting insects. In these instances the poison may be injected into or through the skin. Some of the higher animals like the scorpion and sting-ray introduce their poisons through specialized mechanisms. The venomous animals constitute an important source of poisons acquired in this manner.

Therapeutic agents administered by the hypodermic needle are almost all potential parenteral poisons. They may be introduced intradermally, subcutaneously, intramuscularly, intravenously, or into somatic cavities and bring about local tissue changes or general effects after absorption. Poisoning from these agents arises under the same circumstances as when they are administered through other channels, that is, poisoning occurs when the ordinarily innocuous does proves to be poisonous for the individual concerned or the dose is inordinately excessive through accident, lack of judgment or skill, or is deliberately made so. Intradermal tests employing toxic agents are reactions that are permitted because no serious consequences are anticipated in the amounts used. These reactions may occasionally exceed the expected results and prove to be highly injurious to local tissues or endanger the whole organism.

RESISTANCE TO EXTERNAL CHEMICAL IRRITANTS.

The external cornified layer of the epidermis is an efficient defense mechanism against many of the chemical agents in the environment. Although its outer cell layers are lifeless and cannot partake in defense processes that depend on vital functions its horny nature mechanically inhibits many strong poisons. Keratin, of which it is largely composed, is insoluble in 50 per cent solution of the mineral acids. On the other hand it is soluble in potassium hydroxide even in weak solution.

The stratum corneum is impermeable to water but not to fats with low melting points and oils. This layer is thinnest in infants and therefore more readily damaged by external agents. The corneum of the aged is dry, rough and friable and liable to discontinuities in its surface

The normal skin surface is interrupted by the openings of the hair follicles and the ducts of the sweat and sebaceous glands. These breaks in the continuity of the horny layer are vulnerable points at which irritating substances can come into direct contact with less resistant epithelial cells.

Fatty, oily sebum from the sebaceous glands spreads over the surface of the skin and affords additional protection against those substances which are not soluble in fat or miscible with it. Fat solvents remove the protective film, and oils and fats that have harmful chemicals incorporated in them thus favor absorption by mixing with the natural oil on the skin. The distribution of the sebaceous glands over the body surface is not uniform. They are most abundant in the hairy regions of the scalp and axilla and on the face, shoulders and back.

The resistance of the skin to external chemical irritants is also reduced by mechanical, thermal, electrical, and radiant energy factors, and destructive processes in the skin that have resulted

from pre-existant disease. Variations in normal physiology of the skin may also affect the action of poisons by altering its texture, moisture, blood supply, innervation, oiliness, and pigmentation.

The conjunctiva of the eye possesses little resistance to exogenous chemicals. Alkalies are especially damaging to it. The constant flow of tears across the conjunctival sac, and winking are mechanical factors that operate constantly to dilute and remove foreign matter entering the palpebral fissure. When these protective mechanisms are at fault there is a tendency to dryness of the conjunctiva and an increased opportunity for toxic gases, liquids and solids to remain longer in contact with the membrane cells.

The mucous membrane of the nose consists of ciliated reticular cells. There are numerous mucous glands in the *regio respiratoria*. The membrane is kept moist by the secretions of these glands and tears and secretions coming from the accessory nasal sinuses. It possesses a rich nerve supply which reflexly increases secretions when it is irritated and initiates the act of sneezing.

That portion which is reflected over the turbinates rests on a loose submucous areolar bed which is highly vascular and erectile.

When foreign chemicals enter the nasal cavity in sufficient concentration they call forth a flow of mucus which tends to dilute them and wash them away. The latter is further augmented by the cilia of the cells and sneezing. The hair which is present at the anterior nares acts as a mechanical filter for gross solid particles and fluid droplets. Functional or pathologic conditions which diminish or destroy these protective devices predispose to the action of foreign chemicals entering the nose.

The vagina is lined by stratified epithelium but contains no glands. It is kept moist by secretions from the cervical and uterine glands. The membrane is more sensitive in children and the aged than in the childbearing period because the vaginal mucosa at these ages is made up of fewer layers of cells. Strong chemicals introduced into the vagina can readily produce damage because of the lack of special protecting factors. The cervix is normally closed and impenetrable to solutions placed in the vagina. It may be opened by operative interference and childbirth to such an extent as to permit the entrance of chemicals into its canal or even into the uterine cavity. The columnar and cuboidal epithelial linings of these two structures are rich in secretory glands that aid in the dilution of poisons but may also act as points of lessened resistance and so favor absorption. Almost all substances that can affect the skin may also affect these membranes.

The urethra, bladder, ureter and pelvis of the kidney can only be reached by exogenous chemicals by deliberate instillation. With exception of the diluting effect of the urine and the secretions of glands they possess no natural defense against the action of irritating chemicals.

THE PROCESSES OF DIRECT CHEMICAL INJURY.

When predisposing causes are present which favor the action of a chemical irritant, or the irritant is introduced in such manner and dose as to pass the normal barriers it can enter into direct chemical action with the tissue cells.

In the discussion of the general behavior of poisons it was stated that the chemical reaction with the cells may be of a minor grade that interferes little with the normal functions of the protoplasm and cell processes, or may be so overwhelming as to disorganize the cell and its functions and make its return to normal difficult or impossible.

The most simple form of injury is the extraction of cell and tissue water by dehydrating agents. This results in changes of osmotic pressure and pH concentration which interfere with electrolyte and fluid exchange.

Oxidizing substances may produce more profound effects by altering cell chemistry to a serious extent, and hydrolyzing agents can bring about the formation of materials more toxic than themselves.

Substances such as mercury coagulate albumin and cause profound changes in the physical-chemical state of protoplasm that may terminate in cell death. Strong caustics and corrosives carbonize and dissolve cells and cause their instant death. In weaker dilutions they may fix the protoplasm and bring about complete functional dissolution without causing physical dissolution.

In some instances the poison affects the cellular components indirectly by producing changes in the intercellular fluids. This interferes with the passage of nutrient materials across the cell membranes and results in nutritional failure of the cells, or cell poisoning may occur from the retention of products of metabolism within the cell.

Keratolytics and lipoid solvents produce damage by removing special tissue substances for which they have an affinity. The extent of harm they do depends upon the importance of the dissolved material in the tissue and cell economy.

Instead of interfering with structure and function by destroying cell and tissue elements, a poison may stimulate cells to increased or abnormal activity. Arsenic, coal-tar derivatives and scarlet red can act in this way and produce new growths or accelerated normal cell growth and activity.

THE PROCESSES OF SENSITIZATION.

When a chemical agent comes in contact with tissue cells of a susceptible individual at some time after the cells have had a previous experience with the agent, a series of epiphenomena occur which differ from those resulting from direct chemical action. This

type of reaction is called allergy or hypersensitiveness. It may follow a primary contact which was acquired in the same manner as the second dose, or the agent may have been brought first to the cells by introduction into the body through some other portal of entry. This is well exemplified by tuberculo-protein which sensitizes the cells of the skin even though it be introduced in the form of tubercle bacilli taken into the lungs. At some time later the allergic phenomena occur when a second dose of tuberculin is placed in the skin in making a tuberculin test.

The sensitizing agent is termed the allergen. The nature of the reaction which occurs when an allergen is brought into contact with susceptible cells is still a matter of conjecture. (See pages 181 and 197.) In many instances of apparent sensitization the allergen is not a protein as in the case of plant pollens and foods but a simple inorganic substance.

The connection between non-protein and protein sensitization may possibly be proven to be the development of toxic protein combinations, or derivatives brought about by the action of non-protein poisons on cell constituents, and that this new protein compound constitutes the allergen (Wells). There is always a delay between the time of the first contact of the sensitizing agent with the cells and the appearance of the reaction. Direct chemical action may occur at this first exposure but the allergic phenomena do not appear with a subsequent exposure until this "latent period" has elapsed.

The length of this period cannot be given in any definite units of time for it varies with the sensitizer and the constitutional factors of the individual concerned. It is probable that inheritance factors play a part in some instances and that length and frequency of exposure, concentration of the noxious agent, predisposing factors which favor or retard the chemical union, are all concerned.

The anatomic site of the reaction is of particular interest. Sulzberger[1] presents convincing evidence that oil solvents and substances mixed with or soluble in oils and fats and thereby rendered capable *of easy contact with the epidermal tissues, cause allergic reactions* in the epidermis. This is also made possible by mechanical, thermal and other factors which diminish the resistance of the natural barriers to contact with the epidermis. On the other hand substances which gain access to the skin tissues by way of the blood stream after ingestion or inhalation or which were introduced by some mechanism through the epidermis exhibit the reaction in the vessel walls of the cutis and secondarily in the epidermis. The pathologic lesions of the first group are characteristically a state of spongiosis of the tissues and intradermal vesiculation. In the second group they are extravasation of vascular fluids, edema and the formation of a

[1] Sulzberger, M. B: Jour. Michigan State Med. Soc., 34, 78, 1935.

wheal. Formed elements participate in the reaction with the appearance of infiltrating lymphocytes and epithelioid cells, local eosinophilia, nodular and follicular lesions, and many of the secondary skin lesions.

Immunity to simple chemical skin irritants must at the moment be held *subjudice*, but true immunity must be allowed in the cases of some animal and plant poisons.

The so-called immunity of the "hardened worker" is not permanent for local or general immune substances have not definitely been demonstrated in these cases. Removal of the worker from exposure results in cure but the condition will recur when he returns to his occupation. It is probable that certain local conditions such as actual "hardening" of the skin may reduce the opportunities for the noxa to come into contact with living epithelial cells or that the cells may develop an as yet unexplained refractoriness to the agent. Eller and Schwartz[1] believe that this apparent immunity, evidenced also by periodicity of attack, may be due to the fact that the worker is not always engaged under the same conditions of exposure and that his sensitization may vary with diet, activity, the presence of focal infection and other individual factors. Also, secondary bacterial and fungus infections may complicate and distort the true picture.

PROCESSES OF ABSORPTION.

The absorption of chemical agents through the unbroken skin is limited to volatile substances and those which are soluble or highly miscible in oils, fats, alcohol and ether. Although some of the materials may be taken up by or penetrate the superficial layers of the epidermis by dissolving the oil surface on the skin or going into solution in it, the greater amount enters by way of the less resistant cell coverings of the sebaceous ducts. Water and watery solutions cannot enter through this channel. It is doubtful if alkaloids can be made to penetrate under any conditions.

Technologic processes have developed a large number of materials which are fat solvents and as a result most of these are able to affect the skin locally or be absorbed from it.

The rate of absorption from the skin surface is relatively slow compared to that from the mucous membranes, and the quantitative poisoning that results from the skin is a matter of length of exposure or area of skin involved.

Cataphoresis is the method of carrying ionized materials (medicines) into the deeper layers of the skin on the discharges of an electric current flowing in that direction. It is not highly effective as the amount carried to any significant depth is very small.

[1] Eller, Joseph J., and Schwartz, Louis New York State Jour. Med., 35, 951, 1935.

Vapor baths depend for their efficacy on surrounding the body with heated air carrying particles of volatile substances that can be absorbed.

Any agents which have the power of reducing the normal resistance of the skin or destroying the surface epithelium enhance their ability to be absorbed. Many weak acids, alkalies, and other corrosive and caustic poisons can be absorbed in dangerous amounts in this way.

Destruction of the epithelium by heat, abrasions and other physical *traumatisms open the absorbing areas of the deeper structures* to the action of substances not poisonous to the normal skin.

Beneath the avascular carapace the layers of the skin become progressively richer in lymph spaces, lymph channels and blood-vessels. In these areas any soluble substance can enter the circulating fluids and be carried throughout the body. Very finely divided particles in suspension in the intercellular fluids may also be carried away by the lymphatics. For these reasons general poisoning can occur from absorbable substances applied to the skin.

McCord[1] furnishes a list of substances believed to be able to pass the normal skin barrier:

Ammoniated mercury	Ethylene chlorhydrin	Nitronaphthalene
Anilin oil	Ethylene dichloride	Oleates
Belladonna	Formaldehyde	Olive oil
Benzene	Formalin	Osmium
Benzine	Garlic	Oxides of mercury
Bismuth	Gasoline	Paranitranilin
Boric acid	Guaiacol	Phosphorus
Camphor	Hydrocyanic acid	Phenacetin
Carbon bisulphide	Hydrogen sulphide	Phenol
Carbon tetrachloride	Ichthyol	Picric acid
Chlorine	Iodides	Pilocarpine
Chloroform	Iodine	Quinine
Creosote	Kerosene	Salicylic acid
Cresols	Lanolin	Stoddard's solvent
Croton oil	Lard	Tetraethyl lead
Cyanids	Mercury	Toluene
Cyanogen compounds	Monotrichlorbenzene	Trichlorethylene
Dimethylanilin	Naphtha	Turpentine
Dimethyl sulphate	Nicotine	Vaseline
Dyes (some)	Nitranilin	Xylene
Ether	Nitrobenzol	

The several mechanisms by which noxæ are carried through the skin without touching the superficial layers (inoculation) can deposit the agent in any structure lying beneath the skin. A hollow needle or the fang of a serpent may inject the poison into a lymph space or directly into a blood-vessel. In the latter case it is not a true case of absorption for the materials injected need not be in solution but may be particles in suspension in a fluid medium.

[1] McCord, C P.. Am Jour Pub Health, 24, 677, 1934

When solid particles such as bismuth are injected into subcutaneous tissues absorption and removal do not occur immediately. In some instances the absorption rate is prolonged for days because the chemical must first be transformed by the action of the body fluids into a soluble compound.

The rate of absorption is also affected by the vascularity of the area involved and by the activity of the blood-vessels and lymphatics of the tissues. It is therefore more rapid in hyperemic areas and slower where there is blood or lymph stasis. The physical activity of the organ of which the tissue is a part is also of importance. For example the absorption of a drug injected into an active muscle is more rapid than from a muscle at rest.

Absorption from mucous membranes in general is possible for all substances which are soluble in water and not in a colloidal state. Even the latter may penetrate the membranes and gain access to the submucous structures if the function of the epithelial lining is interfered with. For this reason great caution is indicated in treating mucous membranes with potential poisonous medicaments when disease exists which has damaged the lining cells.

The vaginal mucosa is somewhat more highly penetrable by chemical agents than the skin. This is due in part to the absence of a protecting oil film in the vagina and because the epithelial cells are less cornified than those of the epidermis.

The external ear and auditory canal are well protected by the secretion of the oily cerumen and poisoning by absorption from these structures is rare. The ear drum however is not so protected and may readily be damaged.

The mucous membrane of the rectum is an efficient absorbing surface. This is frequently taken advantage of for medication. The alkaloids and their salts are taken up by this tissue with great rapidity and it is therefore very easy to give overdoses of drugs by this method. Ether and chloroform can be administered by this channel but because it is extremely difficult to regulate their dose precautions must be taken to enable the excess drug to be drawn off at the first evidence of danger.

CHAPTER XXII.

POISONS ACQUIRED BY THE SKIN AND OTHER PARENTERAL TISSUES (CONTINUED).

IN THE TRADES AND INDUSTRIES.[1]

Acetaldehyde.—This is a volatile gas given off in the oxidation of alcohol. It is a conjunctival irritant.

Acetic Acid.—Concentrated acetic acid is a strong corrosive. It is met with as glacial acetic acid in laboratories where burns may result from contact with the skin. The same may occur from monochloracetic acid which is used in the manufacture of indigo. The burn is characterized by a mild pain out of proportion to the extent of the injury.

Acetone.—A solvent widely used in the industries engaged in the manufacture of cellulose products, paints and enamels, perfume, pyroxylin, and dyes. It is a fat solvent capable of producing dermatitis. In the volatile state it is an irritant to the conjunctiva.

Acridine.—Volatilized acridine given off in the manufacture of dyes is a direct irritant to the skin and conjunctiva.

Acrolein.—This is a fuming acrid gas produced in the rendering *of fats and animal and vegetable oils. The gas is produced in the* manufacture of linoleum, glue, varnish, soap, candles, lard, stearic acid, and pyroxylin. It produces a dermatitis and irritates the conjunctiva.

Alcohol.—Prolonged immersion of the hands in alcoholic solutions removes much of the natural oil of the skin and dehydrates the epithelium. This predisposes to drying and cracking of the skin.

Aluminum Silicate.—Produces a dermatitis from its presence in dusts.

Ammonia.—The concentrated gas or strong solutions of ammonia are strong caustics to the skin and conjunctiva by direct chemical action. Poisoning generally occurs from accidents in which the gas or liquid is freed in large amounts from broken pipes in ammonia *plants or refrigeration apparatus. In many industries where* ammonia and its salts are used the possibility of serious ammonia burns is slight. Small amounts of the gas may however produce a troublesome conjunctivitis.

[1] Taken in part from Rosenau, M : Preventive Medicine and Hygiene, New York, D. Appleton & Co , 1935. Originally published by the Bureau of Labor Statistics, Washington, D. C.

Amyl Acetate.—Amyl acetate, or "banana oil," is a cellulose solvent used in the manufacture of many cellulose products and also to dissolve paints, varnishes and shellac. It volatilizes readily and in this form irritates the eyelids. Old workers with amyl acetate appear to get accustomed to its effects.

Amyl Alcohol.—This alcohol like amyl acetate is used in the paint and cellulose industries and produces a blepharitis.

Anilin (Amidobenzene).—In the rubber industry anilin is used as an accelerator in rubber compounding. Opportunities for contact also occur in the manufacture of this chemical itself and in the manufacture of explosives, dyes, paints, varnishes, painters supplies, vulcanizers and coal-tar derivatives. It produces an eczematous dermatitis in sensitized individuals. Anilin formaldehyde produces a similar dermatitis. Hamilton states that this compound along with other accelerators is responsible for rubber itch in handlers of rubber tubes and tires. Anilin black is a fur dye which causes dermatitis after sensitization.

Anthracene.—Anthracence is a benzene derivative used as a dye intermediate. It produces an allergic dermatitis.

Antimony.—This metal and its salts produce a pustular eczema which has been likened to the eruption of smallpox.

Antimony is used industrially in the manufacture of printing type, electric storage battery plates and red rubber goods. In the latter trade the workers become covered with the antimony sulphide dusts. It is also met with among brass workers.

Arsenic.—Arsenic acts upon the skin to produce lesions by direct chemical action and, after repeated contact, by the development of sensitization. In the chronic cases it is difficult to distinguish these contact lesions from the secondary lesions produced by arsenic which has been inhaled or ingested under the same conditions of occupation.

Where arsenic is present in the form of dust the skin lesions tend to appear mostly in the moist areas of the body and where it is retained by the pressure of clothing. Thus they are seen frequently on the scrotum, face, hands, and feet, and along the edges of the eyelids and in the nose. The lesions are at first erythematous in character and later become papular with necrosis and ulceration. Arsenic can be absorbed through the damaged epidermis and contribute to the general poisoning.

Prolonged contact of arsenic with the skin may produce new growths which have a strong predisposition to become malignant.

Exposure to arsenic by contact occurs in the following occupations:

Artificial-flower makers, artificial-leather makers, book-binders, brass founders, briquet makers, bronzers, calico-printers, candle makers, carpet makers, felt hat carroters, chimney sweepers, colored

paper workers, color makers, rubber compounders, copper founders and smelters, curriers, cut glass workers, pottery decorators, dye makers, electroplaters, enamel makers and enamelers, feather curers and workers, ferrosilicon workers, fireworks makers, fur handlers and preparers, galvanizers, gardeners and others using arsenical sprays and dusts, glass mixers, gold refiners, insecticide makers, japan and lacquer makers, lead smelters, linoleum colorers, lithographers, rubber mixers, mordanters, painters and paint makers, paper glazers, paper hangers, paris green workers, pitch workers, pottery workers, pressroom workers (rubber), printers, pyrites burners, refiners of metal, sealing wax workers, sheep-dip makers, shot makers, soot packers, sulphur burners, sulphuric acid workers, taxidermists, tinners, toy makers, velvet makers, wall-paper printers, wax ornament makers, wire drawers, wood preservers, zinc miners and refiners.

Bakelite. (See Formaldehyde.)

Benzene (Benzol).—Benzene is a coal-tar distillate used as a solvent extractor of oils and greases. It is generally employed throughout many of the rubber making processes, in the dye and paint industries, and in the manufacture of artificial leather and fabrikoid.

Due to its solvent action on oils, benzene removes the protecting layer of the skin and causes erythema, vesiculation, furunculosis and ulcers. It is accompanied by a troublesome itching.

Benzine.—This petroleum distillate is mildly irritating to the skin and eyes. For the trades in which it is encountered see Poisons *Acquired by Inhalation: Benzine, page 146.*

Benzyl Alcohol.

Benzylamine.

Benzyl Chloride.—These benzene derivatives are widely used in the rubber industry and the production of dyes, drugs and perfumes from coal-tar. Frequent handling results in an acneiform dermatitis.

Beta-naphthol.—A naphthalene derivative used in the manufacture of para red. It causes a mild dermatitis and can be absorbed through the skin with systemic symptoms of phenol poisoning.

Brass.—The only skin poisoning from brass results from the antimony which is present in the metallic mixtures. See Antimony.

Bromine.—Free bromine is a severe irritant to the conjunctiva and produces a catarrhal conjunctivitis. It is encountered in the manufacture of bromine salts for medicines and disinfectants, in the dye and ink industries, and in the extraction of gold and platinum.

Butyl Acetate.—Used in conjunction with benzene and amyl acetate in the manufacture of artificial leather. It is irritating to the eyelids and conjunctiva.

Butyl Alcohol.—This is a solvent for cellulose, varnish and shellac and is employed in the artificial leather, photographic film, paint and perfume manufacturing industries. It causes an irritating dermatitis with the formation of vesicles. Pustules develop from secondary infection in the damaged tissues.

Calcium Chloride.—Chloride of lime is a constituent of bleaching powders. It is used in the manufacture of chloroform and chlorine disinfectants. Contact with this salt is also met with in its own manufacture. It acts as a caustic on the skin and chlorine liberated from it is irritating to the eyes.

Calcium Cyanamid.—This is a relatively new compound used in the manufacture of ammonia, nitric acid and fertilizer. The dust and powder has a rapid corrosive effect on the skin and even a few hours contact with it will result in a severe dermatitis. It has great penetrating powers and can produce an inflammatory cellulitis which has a strong tendency to necrose and ulcerate. General absorption takes place through the damaged skin which has the effect of producing a dangerous sensitization of the blood-vessels to alcohol.

Calcium Hydroxide.—A caustic alkali which in strong solution burns the skin by direct chemical action.

Carbon Tetrachloride (Tetrachlormethane).—Tetrachlormethane is a solvent for gums, resins and fats and for this reason is used in the rubber industry where it has largely displaced carbon disulphide. For the same reason it is employed as a cleaning fluid to remove oily mixtures. It is an active ingredient of pyrene, a fire-extinguisher.

Although most poisoning results from inhalation of the gas it acts as a solvent of the oil on the skin and produces an erythematous dermatitis. This occurs largely among those using liquid preparations which come in contact with the hands as in cleaning establishments and those engaged in cleaning machinery.

Chlorine.—Chlorine gas is liberated from its loose combination in chlorine salts used as bleaching agents or the manufacture of the gas itself or other chlorine compounds. Any of the industries using bleachers, such as paper manufacturing, present a chlorine hazard. Chlorine in gas or solution is used by photographers, the makers of tear-gas, zinc chloride, bromine, brooms, ink, iodine, disinfectants, rubber substitutes and soda.

Chlorine is an intense conjunctival irritant and produces profuse lachrymation and blepharospasm. It is also irritating to the skin and causes an acneiform eruption called chloracne. There is some doubt as to the true nature of this reaction some believing that it is due to the tar in chlorinated tar products.

Chromium.—Chromium compounds are used as mordants in cloth dyeing and cloth fillers, as a paste on copper plates in photoengraving, in the manufacture of glass, enamel, polishes, rubber

mixers, pigments and dyes, ink, blueprint paper, and other photographer's supplies. Workers come in contact with it in the manufacture of the chemical compounds themselves and in the acetylene and anilin industries.

Chromium is a direct chemical poison to epidermal and epithelial cells and produces tissue sensitization.

On the skin it produces necrosis and ulceration with the formation of deep pits extending into the cutis. These ulcers are commonly spoken of as "chrome pits" or "chrome holes." In the nose the *ulceration may involve the cartilage with marked destruction and* perforation of the septum. The finger nails, knuckles, and toes are commonly affected.

On the larger skin surfaces with less moisture and traumatism it causes an eczematous eruption. It is irritating to the conjunctiva and not infrequently causes chrome sores on the eyelids.

Coal-tar. Dyes.—With few exceptions the finished dyes made from coal-tar are non-poisonous. This is in sharp contrast to the unfinished products which are notorious skin irritants.

Those dyes reported as producing dermatitis in their completed state are Martius or Manchester yellow (dinitronaphthol), Metanil yellow, orange II, sulphur black, new blue R (echtmarineblau), methyl violet and methyl green.

The skin disease probably occurs only in susceptible individuals.

Copper.—Hamilton describes a copper dermatitis caused by an amorphous precipitated copper in a special paint used for covering the hulls of ships.

The skin irritation is of the nature of prickly heat and occurs chiefly on the scrotum, popliteal space, and axilla. It causes some inflammation in open cuts.

Creosote.—Creosote is a mixture of crude phenols obtained from the distillation of wood-tar. Its greatest use is as a wood preservative and termite deterrent.

Contact causes erythema but if it is prolonged there results a superficial necrosis followed by secondary changes in the form of cracks, fissures and pustule formation. Creosote irritation of the hands is met with commonly in bridge and dock workers who handle creosoted piling. Carpenters and builders also come in contact with it in impregnated shingles and wood beams.

Cresol (Hydroxytoluene).—Cresol possesses the same irritating and caustic properties toward the skin and mucous membranes as phenol to which it is closely related. Opportunities for contact burns occur in coal-tar workers, cresol makers, soap and disinfectant manufacturers, dye makers, fumigators, synthetic perfume makers, rubber workers, and in tar distilleries.

Cyanogen.—Cyanogen poisoning, so far as its effect on the skin is concerned, occurs in the manufacture of its compound, cyanogen

chloride, and the use of the latter in industrial processes. Much of the local effect is due to the presence of the chlorine radicle. It produces edema of the eyelids, conjunctivitis and simple dermatitis. Cyanogen compounds are employed in many trades using gold and silver, such as jewelers, gilders, metal polishers, mirror makers, and gold refiners.

Dimethyl Sulphate.—This ester of sulphur is used to make dimethylanilin in the dye industries. It is poisonous to the skin by virtue of its strong corrosive action.

Dinitrobenzene.—Dinitrobenzene volatilizes at room temperature and can be absorbed through the normal skin, producing general poisoning. It is one of the important coal-tar derivatives used in the dye industry and the manufacture of explosives.

The local effect on the skin is a mild dermatitis.

Dinitrochlorbenzene.—This is a coal-tar derivative used in the manufacture of sulphur black. Hamilton states that it has probably caused more dermatitis than any other compound used in coal-tar dye manufacture.

The irritation of the skin first makes its appearance with itching in the bends of the knees and elbows. Erythema and swelling occur from the coalescence of small punctate elevated spots. A similar edema may occur in the eyelids. Prolonged irritation results in eczema.

Dinitronaphthol. (See Coal-tar Dyes.)

Ethylene Compounds.—The oxide and dichloride of ethylene are solvents of fats and oils and are used as intermediate substances in the formation of other solvents.

Ethylene compounds when volatilized produce a simple irritant conjunctivitis.

Formaldehyde.—Formaldehyde as a gas, or in solution as formalin, is an irritant to the skin and conjunctiva. On the skin it acts as a hardener and dryer with the production of a rough dry dermatitis. It may involve the nails and result in almost complete destruction of them. It may produce necrosis of the conjunctiva. There is apparently a sensitization to it which increases with repeated exposure.

Formalin is a common disinfecting solution and dermatitis may *result during its manufacture as well as in its use. It is used in the* manufacture of bakelite and urotropine (hexamethylenetetramine) and severe dermatitis from it is not uncommon in these industries. Formaldehyde is also employed in bleaching and printing processes, etching and photography, embalming, leather tanning, and in the manufacture of artificial silk, rubber, soap, ink, dyes, paper and explosives.

Gasoline. (See Benzine.)

Hexamethylenetetramine. (See Formaldehyde.)

Hydrochloric Acid.—Hydrochloric acid is a strong corrosive acid which produces severe skin burns by its immediate destruction of epithelial cells. (See also Suicidal and Homicidal Poisons: Hydrochloric Acid.)

Burns from this acid may occur in many industries and trades where it is manufactured or in use.

The occupations listed by Rosenau which offer exposure to hydrochloric acid are: acid mixers and recoverers, acid transporters, alkali salts makers, ammonium salt makers, aniline makers, artificial silk makers, dry battery makers, bleachers, bronzers, calico-printers, camphor makers, shoddy carbonizers, cartridge dippers, cement makers, chlorine compound makers, dye makers and dyers, electroplaters, enamel makers, engravers, etchers, fertilizer makers, galvanizers, glaze mixers, glue makers, ink makers, jewelers, leather workers, lithographers, metal cleaners and refiners, paint makers, paper mill workers, petroleum refiners, phosphate extractors, photographers, metal picklers, pottery workers, rubber reclaimers, soap makers, solderers, sugar refiners, tannery workers, tinners, transparent wrapping material workers, vignetters, wire makers and zinc chloride makers.

Hydrofluoric Acid.—This acid is used in etching and finishing glass and in the extraction of aluminum, gold, phosphorus and silicates. It is also employed in bleaching and dyeing processes and the manufacture of fertilizers.

Hydrofluoric acid is a strong caustic and produces burns, necrosis and ulceration of the skin. When volatilized it irritates the conjunctiva and nasal mucosa and if in strong concentration causes necrosis of these tissues.

Kerosene.—Kerosene is one of the heavier petroleum distillates and is used in industry as a general cleaner for the removal of oils and greases on machinery and old type and printing press rolls.

Kerosene cuts the oil of the skin and then irritates the unprotected epidermis. Further changes in the deeper layers of the epidermis result in acne or eczematoid dermatitis. There is a general drying out of the skin due to the removal of the fat as quickly as it is formed by the sebaceous glands. Irritation of the gland ducts may result in the formation of retention cysts, pustules and furuncles.

Lacquer.—Lacquer used in the trades produces an obstinate recurring dermatitis in susceptible individuals. It is a solution of the gummy exudate given off by the lacquer-tree (*Rhus vernicifera*). The solvent is most frequently amyl acetate, benzene or tetrachlorethane. Some of the skin irritation is due to the solvents but there is also an allergic reaction to the lac itself. It is manifested by the development of edema of the skin and the appearance of a papular eruption.

Lacquer dermatitis may occur in those occupied in collecting th raw lacquer or using it in its trade form as a varnish, paint base o filler.

Lead.—The effect of lead on the skin itself is insignificant bu there is evidence that it may be absorbed through the skin an produce chronic lead poisoning. Hamilton states that lead mus be absorbed very slowly but under the conditions in which painter are exposed to large amounts smeared on their hands and arms fo long periods of time it cannot be denied that there is some possibil ity of poisoning.

Mercury.—Metallic mercury in the form of tiny globules ca enter the open ducts of the sweat glands and travel along the hai follicles to the vascular layers of the skin from which they ar carried away by the leukocytes. The mercury may arrive at th skin surface through direct contact with the metal by ore and mercury handlers, or by its presence in volatile form in the air. Mercury impregnated in workers' clothing may rub off on their ow skin or the skin of others who handle their clothes. Volatilized mercury is found in the air around ore smelters and many trade and industries where the metal itself is used, such as in silver plating, mirror backing, gold, silver and platinum extraction, and the filling of thermometers, barometers and other scientific apparatus. Volatilized mercury also affects the conjunctiva.

Mercury salts, if insoluble, enter the skin in the same manner as metallic mercury. The soluble salts exert a direct toxic effect on the living cells and precipitate their proteins. The dermatitis is characterized by erythematous spots which become patchy and eczematous. Necrosis and ulceration may occur after repeated exposures or even a single exposure from a concentrated dose. There is probably some sensitization in the chronic cases and those who exhibit an idiosyncrasy to it. Surgeons frequently are unable to use bichloride of mercury solutions for sterilization because of a disabling irritation of this kind.

Mercury absorbed through the skin and distributed by the general circulation results in mercury poisoning in the same manner as when introduced through other channels. It is eliminated through the mucosa of the gastro-intestinal tract, the kidneys, and practically every body secretion.

A full list of the trades in which opportunities exist for contact with mercury is given on page 156 (Poisons Acquired by Inhalation: Mercury).

Metanil Yellow. (See Coal-tar Dyes.)

Methanol (Methyl Alcohol).—Although it is believed that wood alcohol has no direct toxic effect on the skin it does act as a solvent of the protective fat and so exposes the dry epithelium to other physical and chemical irritants. It is directly irritating to the conjunctiva.

The question of the possibility of absorption through the skin has not been satisfactorily answered. Instances have been reported in which skin contact occurred under conditions which almost completely precluded the inhalation of methanol in toxic concentrations and yet the workmen developed typical poisoning.

Wood alcohol is an excellent solvent for gums, oils and resins and is widely used, though less than formerly, in shellacs and varnishes. The reported instances of skin contact poisoning occurred among users and makers of these materials.

Monochloracetic Acid. (See Acetic Acid.)

Mononitrobenzene (Oil of Mirbane).—Oil of mirbane is a dye intermediate met with in the dye industries. When brought in contact with the skin it is almost immediately absorbed and produces general intoxication. The skin is unaffected.

Naphtha. (See Benzine.)

Naphthol. (See Betanaphthol.)

Nitric Acid.—Nitric acid is a corrosive liquid which gives off acid nitrous fumes when exposed to the air. The acid itself produces a chemical burn with necrosis of the tissues and ulceration. The gas may cause ulceration in the nose and mouth when a worker is exposed to it over long periods of time.

Industrially, the acid is encountered in the manufacture of celluloid, gun cotton, nitrocellulose, nitroglycerine, picric acid and trinitrotoluene. It is also used in etching and metal pickling.

Nitric acid burns generally result from accidents in laboratories or broken or faulty fixtures in industrial plants.

Nitrochlorbenzene. (See Dinitrochlorbenzene.)

Nitroglycerine (Glyceryl trinitrate).—Nitroglycerine produces a dry dermatitis and the formation of rhagades (Rosenau). It is readily absorbed through the skin and produces a general intoxication.

Exposure to this substance occurs in the process of its manufacture and in those who handle the product in filling shells and making munitions and explosives.

Nitrosobetanaphthol.—This substance is used in the production of H acid, and gives rise to a dermatitis.

Nitroso Compounds.—Most of the nitroso compounds are skin irritants which produce a trade dermatitis characterized by erythema and vesiculation. This is attributed largely to their fat solvent action on the skin.

The nitroso compounds are intermediates in the dye manufacturing industry and skin poisoning from them makes up a considerable proportion of industrial claims arising in the industry.

Oils (Cutting and Lubricating Oils) (Coal-tar Oil, Petroleum Oil, Paraffin and Shale Oil).—These crude and prepared oils have a wide use in all industries where fats and other oils and greases are in use or in process of manufacture, and for the lubrication of machinery

in general. Workers among these products can hardly keep fron smearing their hands and arms and often other parts of their bod with the oily substances. Contact with them occurs also in thei own manufacture and in making by-products from them.

If mechanical factors and the effects of other associated chemica irritants can be ignored the oils themselves are still capable of pro ducing lesions in the skin. Most of them however are fat solvent and by thus removing the protecting oils of the skin, leave it dr and open to other factors, such as temperature, traumatism an infection.

The occlusion of sebaceous ducts and accumulation of these fatt materials in the skin form "paraffin lumps." They are not th result of chemical irritation *per se*.

Some of the heavier oils, such as tar and pitch, probably initiat sensitization which accounts for many aspects of tar acne.

An unexplained irritant activity called auxitic action is seen i prolonged injury from tar. It results in the development of plaque and warty growths and occasionally the development of malignan changes (cancer).

Orange II. (See Coal-tar Dyes.)

Oxalic Acid.—This is a caustic acid which produces skin burns but of a less severe character than those of the mineral acids. Redness and blistering are the common results of its direct contact with the skin. In low concentration and frequent exposure it produces a dry erythematous dermatitis. It produces bluish discoloration and brittleness of the nails.

Paraffin. (See Oils: Cutting and Lubricating.)

Paranitranilin.—One of the dye intermediates used in the manufacture of sulphur and azo dyes and para red.

The dust of this material accumulates on the skin and produces a burning, itching eruption. It is capable of being absorbed through the skin and producing serious intoxication.

Paranitrophenol. (See Nitroso Compounds.)

Paranitrosodimethylanilin. (See Nitroso Compounds.)

Paraphenylendiamin. (See Quinone dichlordiamin.)

Phenol (Carbolic Acid).—The effect of phenol on the skin is that of a chemical burn. It results accidentally in industry through defective apparatus or carelessness on the part of the workmen.

Phenol is readily absorbed through the unbroken skin and produces the symptoms of phenol poisoning. This occurs most commonly after large accidental burns from the strong acid. Chronic exposure to small amounts of this acid produces erosion of the skin and eczema. This occurs in the paint, disinfectant and dye making industries and where carboys and containers of the acid are in use and constantly being handled.

Phenyl Hydrazin.—Hamilton records the occurrence of a trade dermatitis among handlers of this dye intermediate in a plant engaged in its manufacture in Germany.

Picric Acid.—Picric acid is used in making dyes, explosives, fireworks, photographers' supplies, smokeless powder and tear gas. Workers coming in contact with it develop an inflammatory dermatitis.

Pitch. (See Oils: Cutting and Lubricating.)

Potassium Hydroxide.—Potassium hydroxide is a strong caustic which destroys the epidermis by softening and dissolving the keratin in the superficial layers, and by dehydration. Burns with this powerful alkali are likely to be deep and persistent.

Potash is used in fat rendering and the making of soaps. It is employed as a bleaching agent and in the manufacture of safety matches and oxalic acid.

Pyrogallic Acid (Pyrogallol, Trihydroxybenzene).—A hydroxy derivative of the benzenes and closely related to phenol. Hamilton states that it is more toxic than phenol but that no poisonings from it have been reported in the United States.

It is used in the manufacture of gallocyanin.

Quinone Dichlordiamin.—Olson[1] states that the dermatitis occurring in the use of fur and hair dyes containing paraphenylendiamin is not caused by this chemical but a mid product called quinone dichlordiamin.

Shellac. (See Amyl Acetate and Methyl Alcohol.)

Sodium Bichromate. (See Chromic Acid.)

Sodium Hydroxide.—A caustic alkali which burns the skin by destroying and dissolving the epidermal cells.

Occasion for exposure exists among artificial silk workers, bleachers and mercerizers, oil refiners, paper makers, soap makers, tannery workers, transparent wrapping material workers and in the manufacture of the alkali itself.

Sulphuric Acid.—A strongly corrosive acid which destroys the tissues of the skin and mucous membranes by its powerful dehydrating and carbonizing action.

Sulphuric acid is one of the most widely used of all industrial chemicals because of its oxidizing and reducing qualities. It also has broad solvent properties which find many applications. Burns from sulphuric acid are generally accidental, or from the effect of one of its volatile oxides on moist skin surfaces.

Tar.—In addition to the production of tar acne and dermatitis (See Oils: Cutting and Lubricating) this heavy distillate possesses some chemical constituents which have a stimulating effect on epithelium. (Wells, Chemical Pathology. Philadelphia, W. B. Saunders Company, 1920.)

[1] Olson, G. M: Jour Am Med. Assn., 66, 864, 1916

Kennaway has demonstrated that the stimulating materials which seem to initiate malignant changes are present in the fractional distillate obtained by boiling at 490 to 500° C. and that they appear to be in the crude creosote oil and anthracene oil complexes.

Experimental cancer can be produced readily in the skin of susceptible animals by the application of tar, pitch and soot under controlled conditions. It is found that all tars are not equally malignancy producing. Of those met with in the industries, Wells states that gas-works tar is most active followed successively by shale oil and petroleum.

Chimney-sweep cancer of the scrotum is attributed to the continued action of mechanical irritation and some chemical constituents in soot.

Rosenau lists the occupations in which exposure to tar and tar products exists as follows: Artificial stone makers, asphalt workers, dry battery makers, briquet makers, chimney sweepers, coal-tar workers, coke oven workers, cord makers, creosoting plant workers, electrode makers, flue cleaners, illuminating gas workers, insulators, tar painters, paint makers, paraffin makers, pavers, petroleum refiners, pitch workers, roofers, roofing paper workers, coal-tar still cleaners, tar workers, and wood preservers.

Tetrachlormethane. (See Carbon Tetrachloride.)

Thallium.—Thallium has been recovered from the dust of ores used in the manufacture of sulphuric acid.[1] The salts of this element are used in depilatory pastes and their manufacture is attended with some degree of exposure to the thallium. A further opportunity for poisoning exists in the incautious handling of thallium poisons used against rats and other rodents.

The use of thallium salts in depilatories and pastes applied to the skin has demonstrated that it can be absorbed through the epidermis and produce systemic poisoning. Damage to the epidermal tissues is represented by the falling out of hair.

Thiocarbanilid (Diphenylthiourea).—An important accelerator used in the rubber industry. The gases of this compound produce a troublesome stinging of the eyes.

Trichlorethylene.—This is a benzene substitute used as a fat solvent in munitions manufacture, dry cleaning and in the rubber industry. It produces a smarting of the eyes and skin and some of the systemic symptoms, mostly of the sensory nerve type, may be due to skin absorption as well as inhalation.

Trichlorphenol. (See Carbolic Acid.)

Trinitrotoluene (T.N.T.).—There are evidences that trinitrotoluene may produce general intoxication by absorption through the skin. This is supported by Cushmann's experimental work on cats, and

[1] Munch, J S.: Jour. Am. Med Assn , 102, 1929, 1934.

the reports on cases occurring in British and American munitions works and in American Dye Works.[1]

T.N.T. has no local effect upon the skin.

Turpentine.—Oil of turpentine is a mixture of oxidized products of terpenes obtained by the distillation of pine resins.

It has a local effect on the skin characterized by hardening, drying, cracking and erythema. It is highly irritating to the eyes and mucous membrane of the nose.

Oil of turpentine is readily absorbed through the skin and produces an intoxication with acute collapse in serious cases and, in milder poisonings, mental confusion, renal irritation with a smoky urine, vertigo, headache, and gastro-intestinal disturbances with nausea, vomiting and loss of appetite. Turpentine is used universally in the paint and varnish industries and trades as a thinner of the slow drying paints, shellacs and varnishes. Contact with the *poison may also occur among art glass workers, rubber cementers,* calico printers, camphor makers, feather workers, linoleum makers, lithographers, millinery workers, patent leather makers, printers, sealing wax makers and turpentine extractors.

Urotropine. (See Hexamethylenetetramine.)

Varnish. (See Amyl acetate, Benzene, Naphthol, Tetrachlormethane, Methanol and Turpentine.)

Wood Alcohol. (See Methanol.)

Xylene (Xylol).—Xylene is a fat solvent which is used interchangeably with benzene and toluene (see above) and in the same industries. Owing to its fat solvent properties it causes a dry erythema of the hands and arms which predisposes to secondary changes from trauma and infection.

Xylene vapor is intensely irritating to the eyes.

Zinc (Zinc Chloride).—Zinc chloride acts as a skin caustic which burns and causes a peculiar ulceration characterized by an undermined whitish eschar of necrotic tissue on a fibrous tissue base. This is said to occur when the skin has previously been broken by some slight injury such as a small cut or puncture wound. McCord and Killner[2] record the presence of such injuries in workers with wood preservatives in which zinc chloride is an ingredient.

[1] Hamilton, A.: Industrial Poisons in the United States, New York, Macmillan Company, 1929.

[2] McCord, C., and Killner, C. H Jour. Am Med Assn., 76, 442, 1921.

CHAPTER XXIII.

POISONS ACQUIRED BY THE SKIN AND OTHER PARENTERAL TISSUES (CONTINUED).

IN GENERAL AND DOMESTIC CONTACTS.

MANY articles of commercial and household use contain chemical substances capable of producing lesions in the skin and mucous membranes.

With the exception of a few caustic alkalies and acids, and irritating solutions, the majority of the harmful materials are incorporated in finished articles. A large number of the chemical ingredients in these articles have been considered in the previous section where they were dealt with as sources of poisoning in trades and industries. In the present chapter they will be discussed from the point of view of the article of which they are a part rather than as chemical entities. Also dealt with in this section are certain animal and plant substances which are poisonous to the skin in either their natural state or after fabrication.

Adhesive Plaster.—The ingredients of the adhesive substance used in adhesive plaster cause an allergic dermatitis in sensitive individuals.

Anilin Dyes. (See Coal-tar Dyes and Hair Dyes.)

Asparagus.—Produces an allergic dermatitis by contact.

Bakelite.—Although the formaldehyde and phenol which are combined to make this product are not in a form to produce injury in the non-sensitized individual, the finished product acts as an allergen to some people and causes an allergic dermatitis.

Bakelite is used to make such articles as cigar and cigarette holders and cases, cosmetic boxes, combs, small boxes and containers, ornaments, and many other common personal and household objects.

Bleaches.—Domestic bleaching agents contain oxalic acid, sodium or potassium hydroxide, acetic acid or ammonia. These are all simple caustics and their prolonged use may produce mild burns or dermatitis. The alkalies remove the oil from the skin and make it dry and rough and predisposed to the action of other irritants.

Brass.—Sensitization to brass is found in individuals who develop a dermatitis under cheap jewelery, such as brass watch cases, necklaces and bracelets. The irritant ingredient is the zinc in the alloy.

Brine.—Cold, strong brine produces a dermatitis in those who immerse their hands in it frequently as is customary with fish dealers and picklers.

Carbolic Acid.—This acid is a common ingredient of antiseptic soaps, vaselines and disinfectant solutions in household use. Some persons are sensitive to even the small amount in these articles and develop a dermatitis from their use.

Severe skin and mucous membrane burns may result from the use of stronger solutions. Strong solutions are highly dangerous when applied within the external auditory canal and vagina.

Cashew Nuts.—Cashew nuts are listed by Eller and Schwartz[1] as *plant allergens.*

Chrysanthemum. (See Pyrethrum.)

Cinnamon.—Produces sensitization dermatitis.

Cleaning Fluids.—Cleaning fluids used for the removal of oil and grease spots from cloth contain such fat solvents as carbon disulphide, kerosene, gasoline or some of the benzene derivatives. Their continued contact with the hands results in a dry dermatitis by removing the protecting oil of the skin.

Oxalic and acetic acids or the caustic alkalies are used to remove rust, ink and similar stains and can produce skin irritation.

Coal-tar Dyes.—Few of the finished coal-tar dyes are poisonous but Sulphur black, Para red, New Blue R and Quinone dichlordiamin (a mid-product found in paraphenylenediamin-containing dyes) produce allergic dermatitis. These dyes are used on furs and woolens especially and the dermatitis occurs where the articles of clothing come in contact with the skin. Such a dermatitis is to be suspected when it is found around the neck in women and on the body or feet of those wearing colored underwear and stockings.

Corn-removers.—Severe skin burns can result from the injudicious use of corn-removers containing acetic acid, bichloracetic acid, nitric acid and caustic potash.

Cosmetics. (See Facial Creams, Lash-lure, Lipstick, Manicuring Preparations.)

Cottonseed Oil.—Cottonseed oil in use as an ingredient of Wesson oil is a potential allergic poison in susceptible individuals.

Cow-parsnip.—The juice of *Heracleum lanatum* produces a dermatitis venenata similar to that of Japanese lacquer.

Daffodil (Amaryllidacea).—Cases of skin allergy are reported among handlers of this plant.

Depilatories.—Barium salts, sodium sulphite and thallium acetate are the common ingredients of commercial depilatories. Their excessive use may result in dermatitis which in hairy regions predisposes to folliculitis.

Dyes. (See Coal-tar Dyes and Hair Dyes.)

[1] Eller, J. J., and Schwartz, L · New York State Jour Med, 35, 951, 1935

Fig (Urticaceæ).—Produces dermatitis in susceptible handlers such as grocers and fruit packers.

Facial Creams.—Cleansing creams contain nothing but inert oils, paraffin and waxes and some scenting materials.

Skin-food creams generally have mercury, salicylic acid or lead incorporated in them. These chemicals are potential irritants to all skins and may also be absorbed through the skin.

Flour.—Wheat flour dermatitis occurs in millers, bakers, and domestic cooks who have become sensitive to it.

Formaldehyde.—This is a general disinfectant used largely in liquid form and produces an eczematous dermatitis. Many persons develop a dermatitis from the least exposure to it.

Freckle Removers.—Commercial freckle removers owe their noxious qualities to mercury or bismuth, each of which is a skin irritant and potential general poison after absorption through the skin.

Fur.—Animal furs possess irritating properties to the skin aside from any chemicals used in their preparation and dyeing. They produce an allergic dermatitis. Fur rashes are more common about the neck where the hair comes in prolonged contact with the skin.

Gasoline. (See Cleaning Fluids.)

Geranium.—Geranium plants cause allergic dermatitis among florists and any susceptible individuals who handle them.

Glue.—Glue produces an allergic reaction characterized by edema in sensitive subjects.

Goat Hair.—Sensitivity to goat hair has been observed in veterinarians and farmers. It produces an eczematous skin reaction.

Golden Rod.—Golden rod dermatitis is caused by the pollen of this flowering plant.

Guinea-pig Hair.—A dermatitis of allergic type occurs in susceptible individuals among laboratory workers, pet breeders and others who come in repeated contact with these animals.

Hair Dyes.—Silver nitrate, aniline derivatives such as paraphenylenediamin, pyrogallol, and henna, are used to change the hair color but in so doing produce in some instances an irritating and often severe dermatitis of the scalp and frequently also of the face and neck.

Oxalic acid and potassium cyanid are sometimes incorporated in hair bleaches and possess possibilities of serious consequences.

Hair Tonics.—The allegedly beneficial ingredients of hair tonics are quinine, lead, sulphur, bismuth, arsenic and salicylic acid in alcoholic or scented aqueous media. Each of these is capable of irritating the scalp and the whole solution not infrequently interferes with the proper function of the sebaceous glands and predisposes to other forms of dermatitis.

Hops (Cannabinacea).—An allergic dermatitis is reported among hop pickers and handlers who have developed sensitization to it.

House Dust.—House dust is a complex of organic and inorganic matter which has become shredded and powdered into a heterogeneous mixture. Owing to the presence of hair, wool, leather and other organic particles it can produce a dermatitis in those who have become susceptible to any of these materials.

Lacquer (*Rhus vernificera*).—Japan lacquer is a gummy exudate of the Japanese lacquer tree in a solvent, such as amyl acetate or one of the benzol derivatives. The gum lac is itself capable of producing dermatitis venenata. Sensitization has been found in individuals who have been using materials covered with lacquer.

Many cases were reported from the use of Mah Jhong counters when this game came into vogue in the Occident. Dermatitis of the gluteal region has been reported from the use of lacquer on toilet seats.

Lashlure.—The harmful dye in lashlure is paraphenylenediamin. In sensitive subjects it produces an itching and burning of the eyes, conjunctivitis, edema of the lids and erythema of the whole periorbital region. Corneal ulcer may ensue and if the poisoning has been intense the process may continue to the point of complete loss of vision and possibly destruction of the eye itself.

Lipstick.—The only potentially irritating ingredient of lipstick is cantharium which may rarely produce a cheilitis with edema. Burnt sienna and carmine are inert so far as harm to the skin is concerned. They are incorporated in a stick made of wax, lard and oil of theobromine.

Leather.—Leather is productive of dermatitis only when it contains some substance capable of causing irritation. Such may be an anilin dye, a nitrocellulose coating, tannic acid, preservative, or various oils or greases used for softening. Leather slippers, and wrist watch bands are the chief offenders because of their close contact with moist skn.

Mango.—This fruit produces an intense pruritus with erythema in susceptible subjects.

Manicuring Preparations.—*Cuticle removers depend for their* effect on sodium hydroxide which acts as a solvent of keratin and softens the cuticle so that it can be loosened from the nail and pushed back.

The liquid nail polishes are colored solutions of benzoin in acetone or cellulose acetate. Some individuals may develop sensitivity to benzoin after a prolonged period of use.

Marigold (Ranunculaceæ).—Dermatitis venenata occurs in hypersensitive individuals who even handle these flowers.

Match Boxes and Matches.—The sulphur ingredient of the striking surfaces of match boxes and the phosphorus in the old fashioned

strike-anywhere matches are skin irritants which produce a chemical dermatitis.

Nettle (*Urtica dioica*).—The stinging nettle causes an itching stinging erythema with urticaria in most persons.

Nickel.—Nickel dermatitis results from the contact of such articles as spectacles, bracelets, necklaces, and watches which contain this metal in an alloy. The commonest nickel alloy in general use is white gold. Dermatitis may also result from the nickel in coins.

Oil of Bergamot.—Oil of Bergamot is sometimes used in toilet waters and perfumes. When it is exposed to sunlight on the skin it produces a disfiguring pigmentation.

Orange.—Orange dermatitis occurs occasionally among fruit handlers and packers. More rarely individuals who are hypersensitive to it develop a dermatitis from peeling a single fruit.

Orris Root.—Orris root is a common ingredient of face powders and is productive of many cases of eczematous dermatitis.

Paint Removers.—Household paint removers contain such solvents as turpentine, acetone, amyl acetate, sodium and potassium hydroxide and methanol. All of these remove the oil from the skin and their use almost demands that the hands at least become saturated. As a result the skin becomes red, dry and cracked. Blistering and mild burns may result in those with sensitive fine skins.

Phenol. (See Carbolic Acid.)

Poison Ivy (*Rhus toxicodendron*).

Poison Sumac (*Rhus venenata*).

Poison Oak (*Rhus diversiloba*).—These three plants contain phytotoxins which have a specific action on the skin with the production of an itching, burning, erythema with vesiculation and edema. The active principles are believed to be complex phenols but this has not yet been definitely proven. Whatever their nature may be they are volatile and capable of being carried on air currents so that highly susceptible persons may develop dermatitis venenata simply by passing in the neighborhood of these plants. Their specific nature is suspected by the development of immune bodies against them.

Primrose (*Primula obconica; P. sinensis*).—Primrose emanations produce an eczematous dermatitis with urticaria. Skin sensitization is believed also to result in a general tissue involvement which reveals itself more particularly in the gastro-intestinal tract.

Pyrethrum (Chrysanthemum).—Pyrethrum powder is used as an ant and vermin deterrent and is burned in antimosquito "incense." Susceptible persons develop a dermatitis from powders, pastes or liquids containing pyrethrum or from the smoke given off when it is burned.

Ragweed.—Ragweed dermatitis results from the deposit of pollen on the skin of susceptibles.

Resin.—Occasional instances of allergic dermatitis are found in handlers of pure resin or resinous woods.

Rouge.—Rouge is a chalk and zinc oxide mixture. It probably rarely produces a dermatitis.

Rubber.—The handling of rubber goods causes urticaria and edema most likely as the result of some ingredient such as hexamethylenetetramine or aniline.

Scourers.—Enamel bowl and sink cleaners depend in part on the scouring effect of finely divided gritty earths and the chemical action of hydrochloric acid, sulphuric acid, and sodium or potassium hydroxide. They are all direct chemical irritants and the last two remove the oil on the skin surface in addition.

Shoe Polish.—The occasional instances of dermatitis brought about by shoe polish are mostly due to sensitization to the acetic acid which it contains or one of the anilin group of coal-tar products.

Silk.—Pure silk produces a hypersensitive dermatitis in persons allergic to it.

Silver Polish.—The danger to the skin from the use of silver polish comes from the caustic action of one of the mineral acids (sulphuric, hydrochloric, nitric) oxalic acid or silver nitrate.

Soap.—The too free use of soap removes the protecting oil of the skin and leaves it dry and subject to other irritating agents. Strongly alkaline soaps may themselves be irritating and carbolized soap may produce a dermatitis venenata.

Timothy.—Timothy pollen produces an allergic dermatitis in susceptible persons.

Toilet Water. (See Oil of Bergamot.)

Tobacco.—Skin sensitization to tobacco is found occasionally among smokers but more often among workers in leaf tobacco and cigar and cigarette makers. It causes a sensitization dermatitis.

Varnish.—Varnish dermatitis results most frequently in those who apply it in a liquid state but some few individuals have such high suceptibility to it that they develop an eczematous patch where their hands or arms come in contact with it on such objects as table and desk tops and other articles of furniture.

Wart Removers.—Wart removers contain such powerful caustics and corrosives as acetic acid, bichloracetic acid, silver nitrate, and nitric acid, all of which are capable of producing severe burns.

Woods.—Wood dermatitis is an allergic erysipeloid response, frequently with vesiculation, from such woods as boxwood, camphor, chestnut, ebony, eucalyptus, lacquer tree, mahogany, redwood, satinwood, teak, Brazilian walnut and rarer exotic woods from the tropics. Although the dermatitis is seen more commonly in those

who handle fresh cut woods and are exposed to their dusts there are those who are sensitive to finished (but not coated) articles made from them. It is frequently repeated that the woods giving rise to dermatitis are mostly of the tropical varieties. Volatile substances from growing trees or particles given off from them may be carried through the air and produce dermatitis venenata without the person coming in direct contact with the tree. Senear[1] in a review of the literature records the suspected noxious principles in the various woods to be non-resinous fatty acids, alkaloids, glucosides, acids, saponins or phenol. They are contained in the saps and resins of different parts of the woody structures including the bark.

Wool.—Wool most commonly produces dermatitis from its use in articles of clothing worn next to the skin. It is a sensitization dermatitis, characterized by intense itching and the appearance of eczematous patches where the clothing is tight. Wool handlers and workers with woolen materials may get eczematous patches from lint which has worked through their clothing or beneath collar and waist bands.

Wheat. (See Flour.)

White Gold. (See Nickel.)

[1] Senear, F. E. Jour. Am. Med. Assn., 101, 1527, 1933.

CHAPTER XXIV.

POISONS ACQUIRED BY THE SKIN AND OTHER PARENTERAL TISSUES (Concluded).

IN MEDICINES AND PHARMACEUTICAL PREPARATIONS.

Individual idiosyncrasy to drugs, their misuse by self-medication, and faulty prescribing and treatment by physicians, account in large measure for poisoning by the application of medicaments to the skin or their parenteral administration. Since all drugs capable of being given by one or more of the methods of injection fall within this classification it is necessary to refer the reader to standard works on pharmacology, therapeutics and toxicology for their fuller consideration.

The present discussion will be limited to the outstanding examples of poisoning acquired from these sources.

A wide variety of pastes, ointments and lotions are put up by pharmaceutical houses and many of them contain substances of a potentially poisonous nature. They can be purchased without prescription and their use is guided only by the directions on the bottle or enclosed circulars. The users are in no position to determine the possible effect of using them wrongly or of recognizing untoward results when they occur.

Arnica Rubs.—Arnica rubs are used for almost all varieties of so-called rheumatic and nerve pains. In susceptible individuals it produces a distressing dermatitis.

Arsenic Pastes.—Arsenic pastes used over a period of time are not only destructive to the skin but initiate malignant changes through the auxitic effect of arsenic. Arsenic may also be slowly absorbed through the skin surface. Arsenic preparations are highly irritating and necrotizing to subcutaneous tissues. Serious consequences may follow the injection of arsenic outside of the vein when attempts have been made to administer it intravenously.

Bichloride of Mercury.—Bichloride of mercury is prescribed or purchased in liquid preparations for general disinfecting purposes and as vaginal douches. Aside from the possibility of general mercurial poisoning following its prolonged use on mucous membranes it produces a dermatitis in those hypersensitive to it. Not infrequently doctors and nurses find themselves unable to use bichloride washes for sterilizing their hands because of the development of a cutaneous reaction.

Mercury in ointments is irritating to some skins. When injudiciously used in large amounts on the skin surface there is a high

probability of developing some degree of general intoxication. While this is being written the author has under observation a man who developed severe mercurialism by rubbing in at one time all of a 2-ounce prescription of blue ointment for the treatment of pediculosis. Mercurialism may result from too large or too intense exposure in mercury vapor baths.

Chrysarobin.—Chrysarobin is prescribed for many varieties of skin lesions but is very irritating to sensitized skins.

Carbolic Acid.—Carbolic acid is dispensed as a general antiseptic and is incorporated in many proprietary disinfecting and sterilizing fluids, soaps, and unguents. Phenol was formerly used for wet dressings on cuts and when left in place too long resulted in carbolic gangrene. Some individuals are sensitive to it in even high dilutions, such as are found in deodorizing and disinfecting soaps. When phenol is applied over a large surface there is danger of absorption with damage to the kidney.

Iodine.—Iodine in the form of tincture or ointment may produce a dermatitis in sensitive subjects. When it is used to disinfect wounds the precaution should always be taken to see that it has dried before it is covered with a dressing as otherwise a serious iodine burn may result. Iodine is contraindicated as a preoperative antiseptic on the skin of patients having an idiosyncrasy to it.

Iodoform Powders.—Iodoform powders are used on vaginal tampons from which it may be absorbed and produce iodism. Iodoform also produces dermatitis in the presence of idiosyncrasy when it is used in dusting powders or ointments.

Formaldehyde Washes.—Formaldehyde washes cannot be tolerated by skins which are sensitive to formaldehyde because of its potentiality to produce a dermatitis.

Novocaine and Procaine Dermatitis.—Novocaine and procaine dermatitis are seen occasionally in surgeons and dentists who are susceptible to these local anesthetics.

Turpentine.—Turpentine in stupes and liniments may be productive of a burning dermatitis.

Chloroform.—Chloroform may cause burns about the mouth and face if these parts have not previously been protected by a mild cream or vaseline before administering the anesthetic.

Butescin Picrate.—Butescin picrate is used in the treatment of burns, and although generally non-toxic, a dermatitis has resulted from its use in a few instances.

IN ANIMAL POISONS AND VENOMS.

Representatives of many orders of the animal kingdom possess secretions which are poisonous when brought in contact with or introduced parenterally into the human body. These secretions are the products of normal physiologic processes and although many

of them can be interpreted as weapons of offense or defense for the organism they need not necessarily be so. Some instances will be reviewed in which the secretions apparently do not serve any such purpose but are casual or accidental poisons for man.

The number of animal poisons is less than the number of species possessing them because some poisons are common to several species or genera. The suspected or proven chemical nature of the poisons will be considered along with the discussion of the different animals. In general the toxic substances are grouped under the single head of *Zoötoxins*. There is a growing belief that true zoötoxins are those which are capable of producing specific antibodies.

Zoötoxins are colloquially spoken of as poisons and venoms, the latter applying more particularly to the poisons of the higher orders of the animal kingdom. They are all poisons by definition.

Cœlenterate Poisons.—The active principles in the stinging poisons of the jelly fish, Portuguese-man-O'-war, sea anemones and coralline hydrozoa have not been positively identified. They all cause stinging or tingling sensations in the skin but the effect of the more powerful ones is better characterized as burning. The pain in some instances is so great as to result in shock.

The effect of the poison on lower forms of animals may be paralyzing but to man they are only skin irritants. In mild stings a punctate erythema develops along the points of contact which in the case of those species possessing tentacles may leave streaks of red perfectly outlining the whip-like filaments. Jelly fish with their poison apparatus on the umbrella-like body leave large red areas. In some species the unknown poison seems to possess a powerful necrotizing effect. The writer has observed burns of this kind from jelly fish in the Gulf of Siam. In them all signs of the injury appear to be well cleared up on the fourth or fifth day whereas a day or two later, the area begins to turn brown and then black and by the end of the week has sloughed out leaving a non-suppurating ulcer which extends through all layers of the skin. No cases have shown evidence of systemic poisoning. In some varieties the poison produces erythema and an urticarial eruption. All severe stings are subject to secondary infection. The stinging mechanism in all of the cœlenterates consists of minute sac-like glands distributed over the body or along the tentacles suspended beneath. The sacs are double walled, the inner layer of which is produced by invagination of the outer layer at the surface end or pore of the sac. The apex of the infolded inner sac is drawn out into a hollow filament which lies coiled up in the space between the two walls. The poison is contained in the fluid which fills this space and therefore bathes the spiral filament.

The outer and inner sacs are called the cnidoblast and nematocyst respectively. The neck of the double cyst projects at the surface of the body and is sensitive to touch. When it comes in contact with

an object such as the skin the cyst is irritated and the nematocyst evaginates and swings the filament like a whip lash against the irritating object. The poison fluid in which it was bathed is thus flung against the intruder. The filaments are very small and can thus penetrate the skin in undefended parts such as the openings of sweat glands and hair follicles or deposit the poison on the skin between the pores.

The more poisonous of the cœlenterates are:

Physalia pelagica—Portuguese-man-O'-war.

Anemone scultatus—A species of sea-anemone.

Olindioides formosa gato—A jelly fish of the Japan waters.

Millepora alcicornis, M. complanata, M. verrucosa—The itchy corals of Malaya.

Rhizostoma pulini—Mediterranean jelly fish.

Rhizostoma cuviere—A jelly fish of the English Channel.

Cyanea artica—A jelly fish common in northern waters.

Arthropod Poisons.—Crustacea.—Crabs possess a toxic secretion which can be introduced into the skin by biting and produces an erysipeloid eruption.

Myriapoda.—The centipedes inject a mildly irritating poison with their bite. Although the poison is described by Bekal and Phisalix[1] as being quinone this has not been verified.

The active principle causes a local itching followed by a red spot which enlarges and turns black. Ordinarily there are no general symptoms but Linceicum[2] has reported a bite from *Scolopendra heros* in Texas which proved fatal to a child of four years of age.

Insecta.—Diptera.—Fleas (*Siphonaptera*) produce punctate hemorrhagic spots at the point of their bite. There may be a mild reddening about them due to hyperemia, and itching.

Gnats and mosquitoes are not known to possess any poisons capable of general effects. Locally their bites are at first hyperemic and then urticarial. There may be considerable edema in individuals who appear to be hypersensitive to them. Itching is a characteristic symptom. Experience seems to point toward the possibility of developing an immunity against mosquito toxin

Lepidoptera.—Poisoning from representatives of this order occur in their caterpillar stage. The noxious material seems to be connected with special body hairs which rub off and penetrate the skin. The reaction is an itching dermatitis with urticaria and sometimes an erysipelas-like rash. Some individuals are more susceptible to this poison than others.

The caterpillars of the following moths are known to be irritating: Brown-tail moth of North America (*Porthesia chrysorrhea*); tiger moth of Angola; various species of *Bombycidea* (silk worm family) and *Limacodidæ*.

[1] Beckal and Phisalix. Compt rend. Acad. sci. Paris, 131, 1004, 1900.

[2] Linceicum, G.: Am. Jour. Med. Sci., 52, 575, 1866.

Hymenoptera.—The *Apiariæ* or bees are stinging insects which inject an intensely irritating poison into the skin.

Flury[1] who has done the most extensive work on the analysis of the poison believes that it is a compound of lecithin with basic radicals from which he has split off choline, glycerol, phosphorus pentoxide, fatty acids and possibly tryptophan and a hemolytic saponin.

The local effect is the production of an area of urticaria and edema with a central point of necrosis. In severe multiple stings and in highly susceptible individuals there may be systemic poisoning with even fatal collapse. Hypersusceptibility to bee poisons seems to exist in some persons while others apparently can develop an immunity.

Bee poison is secreted by poison glands and stored in a sac connected with the stinging apparatus extending posteriorly from the tip of the abdominal segment.

The stinging bees are *Apis mellifica* (honey bee), *Bombus hortorum* (Bumble bee) and *Xylocopa violacea* (wood-bee).

Vespariæ.—The vespariæ or wasps produce poisons apparently similar to the bees (Wells) but their stings are in general more painful and severe. The hornets share the reputation of the wasps. The writer has seen serious collapse in an adult from the sting of 3 wasps (*Vespa orientalis*). General poisoning may also be accompanied by abdominal pain, vomiting and a generalized measley rash.

The species of wasps and hornets responsible for poisoning are: *Vespa vulgaris* (the common wasp of the Occident), *Vespa orientalis* (the oriental wasp), *Vespa crabo* (the hornet), and *Vespa germania.*

Formicariæ.—The Formicariæ (ants) which sting man possess a poison containing formic acid which is largely responsible for the local irritating effects. Flury[2] is of the opinion that there are other substances present and von Furth believes that the poison owes its chief toxic effect to complex poisons of undetermined composition.

The members of the *Poneridæ* and *Myrmicidæ* sting like bees and wasps while the other less harmful varieties secrete an irritating fluid which is injected with their bite.

Ant poisons in general produce entirely local effects characterized by a slightly painful, swollen red area which rapidly subsides.

Arachnida.—The poisonous *Scorpionidæ* (scorpions) inject a poison which has been variously described as neurotoxic, strychnine-like, adrenalin-like and veratrine-like.

Wilson[3] finds that scorpion poison is even more highly toxic to the guinea-pig than cobra venom. He has been able to precipitate the active principles with ammonium sulphate or excess of

[1] Flury, F.. Arch. exp. Path. u Pharm , 85, 319, 1920.
[2] Flury, F.: Ber. d. deutsch. pharm. Gesellsch., vol. 29, h.g., 1929.
[3] Wilson: Bull. Inst. Egypt, 3, 67, 1921.

alcohol and concludes that they are apparently protein and possibly histone.

The stinging apparatus is a caudal spine extending posteriorly from the last body segment. The spine is surrounded by a dense sheath at the apex of which open the ducts leading from the poison gland situated at its base in the caudal extremity. The scorpion strikes by bending its body dorsally and flipping the stinging spine above its back.

Scorpion stings are mostly limited to local redness and edema accompanied by a throbbing pain. The injury seems to predispose to secondary infection.

Severe stings from some of the more poisonous species cause general intoxication characterized by stiffness of the neck, trismus and respiratory paralysis. Some cases show transitory paralyses. Death has been reported, apparently due to respiratory failure.

Scorpion poison appears to be a true zoötoxin for Todd has succeeded in developing an antiserum in horses.

The more poisonous species of scorpions are:

Androctonus funestus—Africa.
Buthus quinquestriatus—Egypt.
Centrurus exlicauda—Mexico.
Buthus martensi—Japan.
Buthus occilans—Italy, Greece, Spain, North Africa.
Scorpio maurus—Egypt.

Araneidæ.—Araneidæ spider poisons are believed to contain hemolytic, neurotoxic and agglutinative principles which are protein in nature and manufactured in parts of the body other than the poison sacs but which are in some species mixed with the relatively inactive secretions of the poison apparatus. The differences in the bites of spiders is accounted for by whether or not the poison ejected with the bite contains these proteins.

The poison sacs are elongated pouches lying in the basal segment of the biting appendages. Their ducts run forward into the hook-shaped distal segments and open at their apices.

As with most of the lower orders of animals the spider bite is largely limited to a local effect. The site of the bite turns red and entirely clears up or in severer types becomes black and more edematous.

The active zoötoxins are apparently absorbed very rapidly into the general circulation. The black widow or button spider (*Latrodectus mactans* and other species) poison produces symptoms resembling an acute surgical abdomen. Collapse may occur and death from respiratory failure is reported, especially in children.

The tarantula bite hardly lives up to its reputation for more recent observations show that in spite of its size and apparent ferocity the effects of the bite are almost entirely local. Its isolated poison has also been found to be less toxic than that of other species (Kobert).

Poisonous species of araneidæ:

Latrodectus mactans—"Black widow," "Button spider" of Southern North American, Central America and Chili.

Latrodectus scelio—"Katipo" of New Zealand.

Latrodectus tredecimguttatas—"Malmignatte" of South Russia.

Theraphosa avicularia—South America.

Theraphosa javanensis—Malaya.

Theridium tredecim guttatum—France and Italy.

Theridium lugubre—Kara Kist of Russia.

Eurypelma steindachneri—American tarantula.

Epeira diadema—"Cross spider." Common garden spider of many countries.

Acaridæ.—The ticks and mites (*Acaridæ*) produce local and sometimes general poisonous effects by the introduction of an unidentified poison during the act of biting and sucking. That of the ticks (*Ixodoidea*) is believed to be protein in nature and capable of producing immune bodies.

Tick bites show as erythematous areas in the center of which are small dark necrotic points which tend to slough out with a disagreeable odor and terminate with the formation of a persistent scar. Large edematous wheals may form around the bite of *ornithodorus*.

The outstanding features of general poisoning are given as fever, backache, headache, vomiting, delirium and convulsions.

The bites of mites (*Ixodidæ*) are limited to punctate erythema with occasionally a more diffuse dermatitis.

Poisonous acaridæ:

Ticks: *Argas reflexus, A. brumpti, A. persicus. Ornithodorus moubata, O. turicata, O. talaje.*

Mites: *Ixodes ricinus.*

Pisces.—Several species of fish possess secretions which are poisonous to man and some of them special mechanisms for injecting it. Although the actual nature of the poison is unknown it appears to be qualitatively alike in all species and a true zoötoxin[1] closely allied to snake venom.

The toxin produces local inflammation with a strong tendency to necrosis of the edematous area. A local paralysis of the part occurs in many instances. Systemic poisoning results in a paralyzing effect on the heart which may be so severe as to prove fatal.

Teleostei.—Castellani classifies poisonous teleost fish on the basis of their poison mechanisms.

I. Fish which poison by their bite.

Muraena helena—In the Mediterranean Sea.

Muraena maringa—In the tropical Atlantic.

Tetrodon fluviatilis—In Indo-China Waters.

[1] Evans, H. M.: Brit. Med. Jour., 1, 73, 1907.

II. Fish which poison by barbs or spines connected with special glands.

Synanceia brachio—(and others)—Melanesian and Polynesian waters. Possess poison glands connected with thirteen barbs on the dorsal fin.

Plotosus anguillaris—Reunion, Malay, India, Seychelles, Abyssinia. Dorsal fin spines.

Sacchobranchus fossilis—India and Ceylon. Poison apparatus connected with pectoral fins.

Thalassophryne reticulata—Panama and Brazil. Hollow barbs on gill covers and on the back close to the head.

Batrachus tau, *B. grunniens*—North American waters and Antilles respectively. Apparatus similar to *Thalassophryne*.

Trachinus draco, *T. radiatus*.

One barb on each operculum and five to seven on the dorsal fin spines. The poison gland of the opercular spine is situated at its base. The dorsal spines each possess two grooves which join near their base to form a conical space. The cells lining this space secrete the poison.

Cottus scorpius—Widespread in Northern Hemisphere. Apparatus similar to Trachinus.

Pterois antennata—Dorsal fin spines.

Pelor filamentosum—Dorsal fin spines.

Acanthurus luridus—Dorsal and anal fin spines.

Selachii.—The selachians possessing poison glands and spines are the stingrays and eagle rays (Suborder—*Raiae*). The dog-fish (Suborder *Squali*) also possess a poison spine.

The active principle of stingray poison has not been determined. It is locally intensely irritating producing a burning agonizing pain, erythema, edema and in severe wounds, necrosis and gangrene. The general effects are shock, syncope and even death.

The stinging barb of the rays are located dorsad at the base of the tail. In some cases the barb is grooved or canalized and connected with poison glands while in others the secretion seems to come from the skin glands and spread on the surface of the barb.

Poisonous species:

Trygon pastinaca—Japan.

Trygon sephen, *T. walga*—India. Gulf of Mexico.

Ætobatis narinari—The "Bishop Ray."

Potamotrygon—Large rivers of South America.

Amphibia.—Few of the species of amphibia are known to be poisonous to man.

The toads (*Bufonidæ*) secrete toxic substances from the dermal glands which Faust[1] has found to be closely related to cobra and crotalus venom. According to this observer there are two principles

[1] Faust, E. S: Arch. f. exp Path u Pharm, 47, 278, 1902.

in toad venom—bufotalin ($C_{34}H_{46}C_{10}$) which is an active digitalis-like substance, and bufonin, a neutral, relatively inactive material which gives the milky appearance to the secretion.

Toads possess no specialized poison apparatus other than these surface glands so that poisoning in man is limited to contact. The secretion is not irritating to the skin but may produce a conjunctivitis if it is rubbed into the eye from contaminated fingers.

Bufo vulgaris and B. agua are representatives of this class of poisonous amphibia. The former is widespread throughout the world and the latter is the large toad of the tropics.

The poisonous secretions of salamanders (*Salamandrinæ*) are also composed of two poisons according to Faust; one an inorganic base, samandarin and the other an alkaloid, samandaridin with digitalis-like effect. The poisonous secretion is discharged on the surface of the body of the salamander from dermal glands.

There is no evidence that these animals can poison man under natural conditions.

Reptilia.—In this class the snakes and the Gila monster alone are poisonous.

Ophidia.—The zoölogical classification places all snakes in this suborder. Within it are found non-poisonous and poisonous varieties, the latter being included in the super-family *Proteroglypha* which is in turn divided into three families: *Elapinæ, Hydrophidæ, Viperidæ.*

The term venom is most commonly applied to the poisons of this group of animals. The venom of all poisonous species are true zoötoxins and are highly active in the production of immune antibodies in man. Investigations on the production of antibodies have revealed a high degree of specificity in that the antivenin against the poison of one species does not protect against poisons from any of the others. Nevertheless there is evidence that the toxic principles are very much alike if not similar and the specificity is due to the attachment of the noxious agents to antigenically specific proteins (Wells). The results of chemical studies on snake venoms have been summarized by Wells (Chemical Pathology, page 140) in the following brief statement: "What has been established is merely that the irritating component of venom can be destroyed by heat, and is removed with the globulin in fractional separations; while there remains a substance not destroyed by boiling, which comes down at least in part with the albumoses of the venom and causes chiefly systemic manifestations."

Earlier studies had revealed that the variation in the action of different venoms might be accounted for by the quantitative relationship between their albumose and globulin fractions. Thus cobra venom contains 98 per cent albumose and 2 per cent globulin, rattlesnake venom has 25 per cent globulin, and moccasin venom

only 8 per cent of this irritating fraction. In keeping with Well's summary this would simply indicate a correlation between the poisonous effects and the proportions of these proteins in the different venoms and not a relationship of cause and effect.

All poisonous snakes possess specialized mouth glands in which the poison is stored. These glands appear to function in a dual capacity by producing some constituents of the secretion through the activity of their own cells and by acting as filters of other toxic substances in the circulating blood and permitting them to enter the gland and mix or combine with its own secretion.

The compound venom has been shown to produce hemolysis and hemagglutination by the action of its hematoxins, immobilization and disintegration of the leukocytes by leukocytolysins, nerve cell degeneration by neurotoxin, and capillary hemorrhage, particularly of the glomerular capillaries, by the action of endotheliotoxins (hemorrhagin) on the endothelial cells.

The degree of intoxication resulting from a snake bite depends not only on the chemical nature of the venom but the proportion between the amount of venomous material absorbed and the size of the body into which it was injected. The amount varies with the quantity in the poison glands when the snake strikes, the amount actually injected, and the efficiency of the absorbing mechanism in the part bitten. Because a snake is not always equally active at different seasons of the year, and because his supply of venom may have been depleted by starvation or recent discharge, the amount which it contains at any one time is highly variable. In spite of the efficiency of the poison mechanism a snake does not always "strike clean" and inject all of the venom possible. If the strike is in a soft vascular tissue such as the calf muscle more venom is likely to be absorbed than from a bite at a location like the shin. It is not surprising therefore that there is great variability in the degree of intoxication from any given bite. An equal dose of venom injected into an adult and a child is much more serious in the child with a proportionately smaller body mass. Further details are discussed under the different types and species of snakes.

Elapinæ.

Naja tripudians—Cobra of India.
~~Naja philippinensis—Cobra of the Philippine Islands.~~
Naja haje—Cleopatra's asp of Egypt and North Africa.
Naja nigricolli—Gold Coast.
Bungarus candidus—True Krait, India.
Bungarus fasciatus—Banded Krait, India.
Bungarus ceylonicus—The Carawalla of Ceylon.
Acanthopis antarcticus—Death adder of Australia.
Elaps corralinus—Coral snake of North and South America.
Dendraspis viridis—Africa.
And others.

The elaperine snakes have well developed fangs which are firmly embedded in the upper jaw and these move only with and as far as the jaw can move. The fangs are grooved anteriorly and the ejaculatory ducts lead from their bases to the poison glands.

Cobra venom acts chiefly systemically, which as has been stated, may be related to the fact that it contains 98 per cent albumose. It contains mostly neurotoxin and poisoning is characterized by nervous system symptoms and little local effect. It also produces much more hemolysis than agglutination.

Krait venom is similar to but weaker than cobra venom.

Viperidæ.

Crotalinæ—Pit vipers.
Crotalus horridus—Texas rattlesnake.
Crotalus scutalus—Texas rattlesnake.
Crotalus confluentus—Pacific rattlesnake.
Crotalus dirussus—America.
Crotalus cerastes—America.
Ancistrodon piscirorus—Water moccasin—America.
Ancistrodon contortrix—Copper head, highland moccasin, America.
Lachesis lanceolatus—Fer-de-lance of Martinique.
Lachesis anamallensis—America.
Sistrurus ravus—America.
Sistrurus miliarius.
And others.

Viperinæ—True Vipers.
Vipera berus—English adder.
Vipera russelii—Russel's viper of India.
Bitis arietans—Puff adder of the Gold Coast.
Cerastes cornutus—Viper of the Pyramids, Egypt.
And others.

The vipers possess a highly developed biting mechanism which is made possible by the structure of the superior maxilla which is narrow antero-posteriorly and triangular with its apex down. From this apex the fangs point downward and backward into the mouth. *The entire maxilla is movable and can be rocked on its base by* opposing muscles whether the mouth be open or closed. As a result the vipers can swing the fangs forward through an arc of some 30 degrees which brings them into a vertical position for striking. When pointed backward at rest most of the fang is covered with a preputial-like sheath of mucous membrane. As the maxilla rotates and the fang is thrown forward the membranous sheath retracts and exposes the fang. The poison groove extends along the posterior surface of the fang. The duct from the poison gland terminates at the base of the fang.

Rattlesnake, moccasin and true viper venoms contain relatively large amounts of globulin, endotheliotoxin and hemagglutinin.

As a result the greatest effects of a bite are of a local hemorrhagic and necrotic nature with a strong tendency toward slough formation and secondary infection. Moccasin and copperhead venoms are more agglutinative than that of the rattlesnake.

Hydrophidæ—Sea snakes.

Hydrus platurus.

Enhydrina valakadien.

Distera semperi.

And others of the genera *Hydrophis, Thallasophis, Hydrelops*, and *Platurus*.

Sea snakes are to be found throughout the Indo-Pacific Oceans. They have no such striking mechanism as the vipers and the mouths of most are so small that they can bite large body surfaces of man only with great difficulty.

Their venom is almost completely neurotropic but is more poisonous than the elaperine and viperine snakes.

Lacertilia.—The Gila monster (*Heloderma suspectum*) of the southwestern United States is the only lizard seriously poisonous to man.

It possesses poison glands at the sides of the lower jaw. Four ducts from each gland terminate in small grooves at the bases of four teeth in the lower jaw.

Gila monster venom resembles snake venom and is largely neurotoxic and has some hemolytic action. It causes death in animals by respiratory paralysis. There is very little local inflammation other than that due to the mechanical injury from the bite.

Mammalia.—Of all of the mammals, the only one possessing any poison toxic to man is the duck-bill platypus (*Ornithorhynchus paradoxus*) of Australia, a single member of the order *Monotremata.*

The poison apparatus of the platypus consists of a movable hollow spur projecting posteriorly from the ankle of the hind leg. A poison gland near its base empties by a short duct into the hollow of the spur. The apparatus is apparently sexual in nature for the female possesses pits on the anterior aspects of the thighs into which the spurs fit during copulation.

The platypus does not attack man with the spurs and poisoning from it is accidental.

The venom contains a poison similar to but weaker than the Australian adders showing mostly neurotoxic effects with slight local action other than pain and swelling.

CHAPTER XXV.

THE DEFENSE AGAINST SKIN AND PARENTERAL POISONS.

Toxic materials acquired by the skin and parental tissues should theoretically be the easiest of all poisons to evade because of the infrequency of mediating processes between the source of the agent and the affected tissue. But this is not true in practice because the source of the poison is often difficult to recognize or the nature of the poison may be unknown or poorly understood. Moreover, since there is great variation in the reaction of individuals to the poisons it is at times highly impractical to expend money and effort to prevent minor poisoning in a few who could be more effectively protected in other ways. In ordinary life the same difficulty is met with in the sensitization to fabricated articles which it would be foolish to dispense with just because some individuals were affected by them.

Prevention on a large scale can only be accomplished by intelligent understanding of the nature of the poisons to be dealt with and the manner in which they are acquired. This, in the main, is the province of Industrial Hygiene.

Within the industries the producers know the materials which are used, the chemists know their properties, the technicians the processes in which they are involved, and the workers are aware of the conditions under which they work and the effect of the materials upon them. The Industrial Physician is faced with the responsibility of protecting the health of the workers and the interests of his employer. He is above all a physician in practice and as such is engaged in the care of his patients and the prevention of disease in others.

Although the producer is legally responsible for harm acquired in the manufacture of his product and wishes to protect himself against loss of personnel and the payment of claims he is not necessarily *capable of accomplishing this protection without medical aid.* In the zest for turning out new products and acquisition of new materials and processes it is not surprising that the management and engineers should overlook the possibilities of harm to their employees. The Industrial Physician alone has the broad point of view which is needed for adequate protection to the worker. He should be consulted on all matters pertaining to the health of those under his charge and this must include informing him of what materials are in use or contemplated to be used in the processes.

The salvage of by-products has materially reduced the amount of materials formerly allowed to go to waste frequently in a manner hazardous to the workers. Irritant gases, dusts, fumes and liquids which once were permitted to be discharged openly in the air are now confined and put to use. Inestimable numbers of contact poisoning have probably been prevented by this advance.

Technologic advances in machinery and equipment should still further reduce the possibility of workers coming into contact with skin poisons. Where ores and irritating liquids were formerly carried in open containers by hand, wheelbarrows or trucks, they are now removed by mechanical conveyers The whole tendency is toward "closed methods." Distillates and residues are carried off by suction in closed cylinders, towers, and pipes to the next process without any possibility of contact with them.

While most of the above improvements are being introduced into the larger industrial plants the small producers are forced for economic reasons to continue with old processes. Unfortunately, these do not have the advice of their own industrial physicians and the workers continue to be exposed. It is in this class that the Workmen's Compensation Act will eventually do most good. The large firms improve technics mostly for immediate gain, the smaller ones will be forced to add protective measures to prevent indirect loss through undue compensation payments and general inefficiency of sick employees.

In the small trades and individual occupations the handlers of harmful materials have little benefit of indirect protection and must rely on their own efforts. The photographer and engraver who is constantly using corrosive acids can only escape injury by caution which he has learned through painful experience or forewarning from others. Less obvious instances of skin irritation are found where there is little obvious connection between the injury and the cause of it. This is the common story in most of the occupational dermatoses in men who consult a private doctor for some skin disease which they do not connect with their occupation. The millions of cases diagnosed as "eczema" attest to this fact and the failure of the physician to recognize the cause. Prevention here is prevention of continued irritation. Since the disease persists only so long as the irritant is present the adoption of protective measures is real prevention.

A considerable amount of occupational dermatitis can be prevented by adequate examination of applicants for employment. Any history or evidence of an allergic condition should be a warning that he may be an easy subject for skin or other sensitization under the conditions in which he will work. With such forewarning he can be instructed as to the nature of the materials he will use and how to protect himself from them. The use of gloves, hand lotions

and creams, personal cleanliness, care of the mouth and eyes, protective clothing, habits of eating at lunch are all practical, sound methods of protection for the individual workers. It is at this time too that he should learn to report early to the physician or other responsible officers when any dermatitis, conjunctivitis, or other evidence of poisoning makes its appearance.

Sanitary codes, official inspection service, nuisance acts and employer—employee agreements all play important parts in reducing the health hazards of occupational dermatitis and absorption of harmful substances.

The contact poisons of every day life present a long list of materials to which the average citizen is exposed. These substances have little in common other than the ability of many to induce allergic reactions in susceptible individuals. Some of them, such as oxalic acid and potassium cyanid in hair lotions should be legislated out of existence, others like lye, potash, caustic acids, and phosphorus should carry adequate warning labels and poison signs. Prevention against them would then rest on individual intelligence and caution in their use.

Until children, youths and adults are educated to the potentialities for harm in the common commercial and household objects, and until they become habituated to the idea of presenting themselves to doctors for health examinations while they are well, the only hope of preventing sickness from these causes lies in educating them to go to a doctor early when they are sick. In this way the physician having diagnosed the condition and pointed out the connection between cause and effect, can at least instruct the patient how to prevent a recurrence. The latter can be accomplished by avoiding the responsible substance completely or by substituting something else for it; by giving up the use of hair dyes, cosmetics, dyed cloth, furs, etc.; by the use of protective gloves or other clothing under conditions of exposure; and by desensitization against the specific allergen whenever possible.

It is to be hoped that medical propaganda will force out of use some of the ingredients of articles of trade which are harmful to any considerable number of people. The private practitioner can aid greatly by reporting instances of such poisonings to his colleagues and other interested parties.

Potentially poisonous ointments, lotions, antiseptics and so forth will always remain so as long as they are used for self-medication. The laity cannot be expected to know all of the dangers inherent in self-medication and must be taught. This can best be accomplished by prohibiting the sale without prescription of the most harmful substances; by proper labeling of all potentially poisonous skin applications and medicines for external use; and by general propaganda against using them without medical advice.

The production of skin irritations, burns, and general poisonous effects from substances applied to or administered through the skin may be classed as therapeutic accidents. To avoid them, the physician must not only employ his best skill but must know his patient. Because patients differ in their susceptibility to drugs it is imperative that physicians adopt no therapeutic rules-of-thumb, but regulate the dosage, manner of administration and selection of the medicament to be used, to the individual factors of their patients.

Because the woods which cause dermatitis are more likely to produce injury in the industries and trades prevention of poisoning from them rests on the principles outlined at the opening of this chapter. For those who are sensitive to them in fabricated articles prevention is the same as for commercial and household objects.

Exposure to plant poisons is most commonly through accidental contact with them in their growing state. Poison ivy, oak and sumac grow wild and are frequent nuisances about farms and in woods. They should never be allowed to grow in home gardens or public parks. Children especially need to be protected from them.

The poisons of flies, mosquitoes, ticks and gnats are little more than irritating nuisances but even as such should be combated by general sanitary control measures, the screening of homes, and individual precautions.

The defense against the venoms of higher animals is understanding of the natural history and behavior of the individual species. Children should be taught the nature of poisonous animals; what they are, where they are found, and how they act.

Sportsmen, farmers, veterinarians, zoölogical garden attendants, scientific collectors and explorers are the most liable to be bitten by venomous animals and must know the fundamental precautions to be taken against them.

Specific preventive inoculation of antivenin may be a possibility but has not yet reached the stage of practical application.

Knowledge is the main defense against all poisons within this category. After it, comes precaution and skill in handling harmful objects, and lastly the protective measures raised by group effort against the lack of knowledge and understanding of the few.

CHAPTER XXVI.

CATEGORY IV: PHYSICAL FORCES AND ENERGIES.

GENERAL CONSIDERATIONS.

SINCE the human organism possesses mass and extension in space it is subject to all of the forces and energies which affect physical bodies. From its earliest single cell stage it is influenced by its physical environment and develops under the necessity of adapting itself to the mechanical stresses and strains of the structures immediately contiguous to it and to other forms of energy.

This applies to every part of the developing organism; the primitive cell layers are as much influenced by their neighboring cell structures as the whole embryo is by its enveloping fluids and membranes, and each of these primary tissues is affected by its neighboring cells and intercellular substances.

Physical growth is attended by increase in mass and dimension *and this must result in a constant disturbance of the equilibrium* between the growing body and its spatial relations; the usurpation of space formerly occupied by other bodies calls forth a resolution of the disturbed equilibrium by readjustment; the total physical state as to its position, size, shape, mobility and other physical characteristics may be looked upon as a resultant of its internal and external environmental forces. For growth to proceed in any direction the energies of the growth process must exceed the forces which oppose it. For example, the increase in size and number of cells will necessitate that the growing part extend itself within the gravitational field, always conforming to the laws of gravity, but it is to be noted, not necessarily in the direction of gravity. It may be inferred therefore that the growth forces exceed the "pull" of gravity and permit the organism to extend itself within the scope of its other limiting factors.

The most immediate limiting factors are static and kinetic mechanical forces that express themselves as pressures, stresses, strains, and tensions imposed on the growing body by physical structures surrounding it. But again, observation shows that growth goes on successfully even under such opposition.

It cannot be inferred from this that the energy of growth is the only positive factor involved. It may well be that normal growth would not proceed in the absence of normal opposing forces and that the organism excels because its hereditary endowment requires it to develop under conditions that positively enhance and direct it.

Additional energies influence the body throughout the postnatal periods. Barometric pressure, humidity, electromagnetic forces, fire, wind-pressure, temperature and sunlight are further embodiments of energy under which life proceeds. At no instant of waking or sleeping existence is the body ever free from these external forces, or of the physical relationships between cells, tissues, and organs. As the organism increases in complexity and the colonies of cells become differentiated into tissues and organs, it results in a multiplication of the physical forces operating between the related parts and a larger total mass in relative equilibrium with its physical environment.

From the standpoint of the postnatal period with its independent activities of locomotion and other complex purposeful movements the embryonic stage is relatively quiescent. For example, the ends of long bones may be in close approximation while the joint surfaces between them are being formed but the stresses on the articulation are slight compared to the forces of weight-bearing and active motion in the adult; the balance of the opposing flexor and extensor muscles of the fetus have not been put to the test to any degree comparable to the requirements for maintaining the upright posture; changes in intra-abdominal pressure are almost minimal up to the time of birth whereas after birth this pressure is subject to additional forces which result from breathing, bending, weight-lifting, coughing and similar physical activities; the arches of the foot of the infant are entirely unfamiliar with the need later to be imposed on them of supporting effectively a 150 to 200 pound body.

Specific heredity supplies the structural means in anticipation of their use. It prepares organs and tissues to meet the needs of the future by directing their growth in such a way that they can develop and maintain a state of relative equilibrium against a series of repeated stresses and strains. In the normally developing body these strains are within the limits of physiologic tolerance and the mechanisms do not break down. The movements of the kicking, turning, crawling infant for the first year of life permit the knee structures to develop under small increments of physical demand and mature to the point of being able to meet the needs of standing and walking when the time arrives.

The sum total of the physical adjustments and adaptations of the human organism to the internal and external mechanical factors of its environment is Body Mechanics, better called, Body Dynamics. This is a complex of mechanical forces and encompasses far more than the ability to stand upright against the force of gravity and to undergo certain limited postural and progressive movements. In its broadest sense Body Dynamics embraces these and more; it includes the pressures within the body cavities, the movements of organs, the static pressure of organs on each other, the tensions

on suspensory ligaments, the limited movements of the different kinds of joints, hydro-statics, the changing volume of organs and their contents, the architecture of the bony framework, patterns of movements, accommodations and compensations between parts, muscle balance, coördination of functions, tensile strength, breaking points and elasticity of tissues and the relationship of all of these to automatic and voluntary control.

Many of the physical forces and energies operate co-incidentally with the factors embraced in the other etiologic categories as necessary elements in the growth and development of the body. In this rôle they play the part of agents essential to normal organization and function and are therefore important factors in health.

Whatever the nature of a physical force that is applied to living substance may be it acts by merging with the physical-chemical activities of the cell and must become a physical component of the cell. Thus, no matter how close the external physical factor may approach the organism it can produce no effect until it has entered into the energies of the part on which it acts. It is important then to conceive of the physical agents as arising externally to cells and cell groups but operating internally within their organization. For example it is an error to think of prolonged pressure on a tissue as something which simply pushes it aside and that the tissue is therefore only passively displaced. If one organ out of place presses on another in an abnormal way the pressure forces are transmitted throughout the second organ and may interfere with the structure and functions of its parts. Excess heat causes molecular disturbances within cells; radiant energy enters into and bombards the molecules and atoms; direct trauma disrupts tissue and cell organization.

Normal cell function requires a variable measure of each of the physical energies. Body cells carry on their functions with optimum efficiency within a limited temperature range; cells exposed to visible light are adapted to rays of certain wave-lengths and intensity; the cells of the arterial vessel walls function best under limited tensions of the tissues of which they are a part; tissues of joint surfaces are adapted to limited pressures.

But what may be favorable to one tissue or cell may be harmful to another. Evidence that what can be tolerated by one organization may be intolerable to another leads to the inference that tolerance to physical forces varies with different organizations and is a matter of degree within any one organization. The realized adult body is therefore a complex of differentiated lesser organizations each of which is best adapted to function under the influence of those energies which have shared most actively in its development.

As has been pointed out in the earlier chapters it may be assumed that there is a limit of tolerance to physical agents in all organiza-

tions. This limit lies between the sphere wherein the organization can successfully adjust itself to physical agents to which it is exposed, and that sphere characterized by the inability of the organization to cope with untoward expressions of familiar forces or intolerable amounts of new forces with which it has had no previous experience. Thus, although a tissue has been under the influence of electro-magnetic forces since its earliest inception it is not prepared thereby to withstand the excesses of a severe electric shock, nor is another tissue which has been exposed to pressure traumatism over many years any the better able to resist the destructive action of a sudden blow. In both of these examples, and in all other instances which can be studied, it will be found that the limit of tolerance is that point at which the equilibrium has been disturbed beyond its power of independent readjustment within its accustomed functions This does not imply failure of readjustment but indicates only that unfamiliar activities beyond those ordinarily concerned must be called upon to help the organization or function restore its balance. It is the appearance of these unfamiliar types or degrees of activity that gives the only practical understanding of what at present is meant by abnormal.

Since it can be demonstrated that physical energies can disorganize functions within cells, tissues, organs, and the body as a whole, all of the forces included within this category can act as etiologic factors in disease. These differ from the factors in the other categories by their modes of action in that they enter into the fundamental physical relationships of the elements of the object they attack. Exogenous chemical agents, hereditary factors and elements of nutrition also depend ultimately on physical factors for their effects but they are larger embodiments of energies and operate at higher physico-chemical levels.

CHAPTER XXVII.

THE MECHANISMS OF MECHANICAL FORCE.

INTERNAL MECHANICAL FORCE.

(Body Dynamics.)

It has long been the custom to consider the human body as a machine and this has been strengthened by the current materialistic philosophies. If life processes are looked upon as being purely mechanical then it may be valid to conceive of them as machines. But the living substance in which these processes are realized possesses an organization and activity which surpasses any notion of a mechanical contrivance. No machine as it is ordinarily understood possesses the powers of growth, development, repair and reorganization evidenced by living tissue. Within the narrow confines of a structure containing certain mechanically moving parts activated by natural sources of energy for the performance of some useful effects the human body acts like a machine. But the cells which are the structural units of the body are processes which are continually undergoing changes of a non-mechanical nature. In so doing they may manifest some evidence of mechanical action but this does not make up their whole nature. The organization of the body as a whole shares in the non-mechanical nature of the cells but uses mechanical forms for the performance of certain of its functions. In essence it is a complex physical organization some parts of which act together as a machine.

Body dynamics is the study of the body in its machine-like aspects. The examination of the forces operating between its parts under conditions at rest or equilibrium is Body Statics and while exhibiting the phenomena of motion is Body Kinetics. The idea of the mechanism or machine connotes too much of the kinetic phase and for this reason the term Body Dynamics is used instead of the more restricted conceptions in Body Mechanics.

Analysis of the dynamics of the human body requires the frequent use of the word force which is commonly considered to be of the nature of a push or pull. In this discussion the idea of force will conform to that of the newer conception of physics that force "acts as though" it pushed or pulled. Thus the "pull" of gravity is not considered as the result of a real pulling toward the earth but as the effect of gravity on mass which acts as though it pulled it downward.

Throughout his phylogeny and ontogeny man has never been free from the tendency of every particle of his body to press downward toward the center of the earth. When he stooped, as it is believed he did in his Neanderthal days, his balance was not as it is now; his knee, ankle, sacrovertebral and other joints could not have had exactly the same angles and plane relationships as those of modern man. In his ontogeny man changes from the prone to the erect when he learns to walk and shifts acutely the stresses on those structures which must retain certain of his parts in their normal position. If later in life other factors affect him and weaken supporting structures, his organs will droop in the direction of gravity. Prolapse, visceroptosis, flat foot, and varicose veins are a few organic changes in which this phenomenon has become evident.

Since gravity itself is not a force it cannot be a cause of disease. In any instance in which it appears that a structure is being pulled out of place by the "force" of gravity it must be understood that it is displaced only as the result of a shift in the equilibrium between its mass and forces opposing it. Under these circumstances the mass then moves in the direction of and in obedience to the laws of gravity. Gravity never increases of itself and causes a body in equilibrium or rest to shift its position.

Body Posture.—The human body is constructed on a movable bony framework of a genetically adapted type which permits wide varieties of posture. It also possesses mechanically acting structures which maintain the functional and anatomic relationships of the parts of this framework and activate its movements. Normal body posture may then be looked upon as those positions which conform best to the anatomic form and physiologic activity of these mechanical structures as determined by their phylogenetic characters. The latter alone account for the difference in posture between man and beast, and in each the normal posture is a satisfaction of the genetic requirements.

Any number of postures is normal for man. The normal for the standing position without motion is erect with the chin slightly elevated, the curve of the cervical spine smooth with the head slightly retracted, the sternum high and the shoulders squared, the lumbo-sacral curve gently concave, the arms hanging easily with slight flexion at the elbows, the pelvis at an angle that follows, without straining, the lumbo-sacral curve, the lower abdomen retracted, the legs straight, the heels close together and the great toes slightly separated from each other. In this position the anatomic relationships of joint surfaces are at their best, flexor and extensor muscle groups are in equilibrium, ligaments and fascia are under minimal strain, visceral alignments are normal, the projection of the center of gravity of the body will fall within the area

The normal sitting posture is determined by the same factors which operate to produce normal standing posture. Sitting always means a shifting of the supporting base to structures about the pelvis and the nearby elements of the upper leg and lower spine. All normal sitting positions must comply with the requirements that the mechanical structures concerned are not forced beyond their limits of physiologic endurance. If the object upon which the base rests gives such support to bones, joints, ligaments, tendons and muscles as to relieve them of strain then even a non-erect and apparently slouching position must be considered normal under the circumstances. It is when there are no subsidiary supports such as back rests, pillows and arm rests that the erect sitting posture is the only position in which equilibrium is obtained with the least physical strain.

Any movable part or all of the body may depart from these norms and take up other positions which are normal provided the direction, distance and force of movements do not exceed the functional and structural limits of any part. All of the accustomed actions in standing, running, jumping, sitting and lying down are carried out by normal movements of parts without harm to them or to their associated structures, such as viscera, blood-vessels, and nerves.

The Causes of Faulty Posture.—Since faulty posture is only the evidence of change from the normal relationships of body parts and is itself a process it must necessarily have been produced by antecedent causes. In this sense faulty body posture is not an elementary categorical factor in the etiology of disease and its causes must be sought among the elements of the categories.

Inherited Factors.—Any inherited disease or structural abnormality which affects the form, configuration, or strength of any part or parts of the bony framework or the normal relationship between them, or influences the functional activity of the muscles, tendons and ligaments will alter posture. Among the bone conditions may be listed extra vertebræ and fewer vertebræ than normal, cervical rib, supernumerary, too few and webbed toes, short first metatarsals, posteriorly placed sesamoid bones of the feet, club-foot, achondroplasia, synarthroses, fusion of bone, absence of bones and hereditary diseases which influence their ossification and growth. The diseases affecting muscle function which have a hereditary etiologic basis are myasthenia gravis, hereditary ataxia, pseudohypertrophic muscular paralysis, multiple sclerosis (possibly), myotonia, Gower's muscular atrophy and defects involving the fascial planes and connective tissue structures related to the muscles.

Acquired Factors.—An acquired factor is one which influences the germ plasm, or the zygote which develops from it, in any manner other than through the normal processes of inheritance. The time factor as to whether the influence occurred before or after birth is immaterial to the definition and only serves as an opportunity

under which the cause can produce different kinds and degrees of change. The term congenital implies only that the condition antedated birth and should never be used to connote inheritance.

All acquired factors which can produce faulty posture must be included in the nutritional, exogenous chemical agent, physical force and energy, parasite, and psychobiologic categories. Information on the primary etiologic factors responsible for the development of many prenatal conditions is too inadequate to theorize with much accuracy on the cause of these defects and it is necessary to be content with a few postulates based on some observed clinical and experimental facts.

The nature of acquired conditions which produce faulty posture and mechanical defects is the same as that described under inherited factors. That is, they are structural and functional defects which interfere with the normal balances and mechanical relationships between parts.

From the studies of Mall[1] on the origin of developmental defects in faultily implanted ova and the researches of Stockard[2] on vertebrate embryology it has been conclusively demonstrated that environmental factors can influence the development of particular parts of the embryo. Stockard, through his own experimentation and the interpretation of Mall's findings has concluded that any factor which slows the rate of development of a part at that moment at which the budding and growth of the part is at its most critical stage will result in arrest of growth and deformity. If Stockard is correct in his deduction that in the human the only general environmental factor which can operate to cause slowing of the rate of development is want of oxygen then any influence that favors oxygen lack can be the cause of malformations. Stockard and many others agree that delayed implantation of the fertilized ovum, implantation in less favorable parts of the tubal-uterine canal than the ordinary sites of attachment, improper chorion and placenta formation due to disease of the uterus, and chemical poisons acting on the whole embryonic structure, can interfere with the rate of growth of the whole embryo and thus produce local arrests of any parts which are at their critical stage during the time that the factor is operating. Thus a number of primary factors may act to produce the complex processes which interfere with the rate of growth.

A second group of acquired defects, which may still have part of their mechanism in inheritance, includes those characterized by intra-uterine amputation. It is no longer believed that these are due to constricting amniotic bands but are accounted for primarily by developmental arrest or cytolysis and histolysis of poor biologic material. It is in the latter that the influence of heredity is believed

[1] Mall, F. P.: Am. Jour. Anat., 22, 72, 1917.
[2] Stockard, C. R.: Am. Jour. Anat., 28, 115, 1921.

to play some part. Obviously a body born with a part or the whole of some necessary mechanical feature missing, such as the foot or arm, will result in compensatory changes in posture.

Total or partial deficiency of nutritive elements can produce structural and functional mechanical abnormalities by interfering with the processes of bone, muscle, fascia and nerve physiology.

Malnutrition in general is considered by most authorities to be equal to or of greater importance than faulty habits of sitting and standing in the development of bad posture. A weakened musculature fatigues more readily than one in good physiologic activity and thus fails to retain the body frame in its normal position. Under fatigue the head hangs forward, the shoulders droop, the trunk sags and permits the bodies of the vertebra to rotate and produce scoliosis, kyphosis and lordosis, the lower abdomen becomes pendulous, the calf muscles and supporting tendons and ligaments of the ankle and foot lose their tone and allow the foot to pronate and the arches to flatten, and the whole body assumes the posture of a "flexor slump." Under such conditions it takes almost too much willful effort to straighten up into the position of physiologic balance and the tendency is to establish a new equilibrium in the faulty position.

Defects of special nutritive elements are exemplified by rickets and beri-beri. In these the bones, muscles and nerves are involved to such an extent that they either cannot tolerate the normal stresses placed upon them or cannot properly perform their accustomed mechanical movements.

Overactivity or underactivity of the glands of internal secretion may so alter the general size and conformation of the body as to interfere with its normal attitudes or may produce disproportions in its parts and bring about faulty postures. Other metabolic changes and diseases which disturb the architecture and strength of bones can lead to mechanical defects such as curving of bones (Paget's disease), spontaneous (sic) fractures (Fragillitas ossium) and dislocations under stresses which would ordinarily be tolerable to normal tissues.

Infectious agents such as the tubercle bacillus actually destroy bone and cartilage and produce permanent deformity. Or micro-organisms may invade muscles, tendons, ligaments, fascia, and nerve elements and profoundly affect their mechanical efficiency. Chronic infectious arthritis, myositis, thecitis, synovitis, peri-arthritis, poliomyelitis, Charcot's joint and other trophic changes following nerve infection, and spinal cord diseases are examples of the conditions affecting body mechanics which result from the action of invading organisms or their poisons.

Fracture, crushing and dislocation of bones, and nerve, muscle, tendon, and fascia injuries resulting from external traumatic factors

are common causes of temporary or permanent postural deformities. More static external forces are the abnormal stresses caused by ill-fitting shoes, high heels, constricting articles of clothing, prolonged pressure from splints, crutches and other mechanical contrivances, foreign bodies within the tissues and occupational stresses from continued standing, the assumption of strained attitudes, the constant repetition of movements and the prolonged pressure of instruments and tools on susceptible parts. In the absence of organic disease either the conscious effort to assume correct attitudes or the acquisition of good posture habits are the most important factors involved in maintaining the body in normal mechanical efficiency. Conversely, the failure to establish wilful or habitual practices of good body mechanics is an outstanding cause of faulty posture.

Even in the presence of undernourishment or subjection to prolonged and excessive strains the assumption of good postures and the avoidance of clumsy, awkward and strained mechanical movements lessens fatigue. Because fatigue reduces mechanical efficiency poor posture predisposes to bad posture and sets up a vicious cycle.

Defects in two of the special sense mechanisms are common causes of faulty posture. In children especially, the inability to hear or see well produces strained attitudes. A partially deaf child almost always turns the head to one side in order to catch the sounds more effectively and contorts the body to compensate for the strained position. Children with defective vision lean far over their desks to bring the book or paper within their focus. Fatigue soon makes it necessary to relieve this strain by rotating the body in some way so as to bring support or relief to the tired back. The repeated assumption of these positions makes it easy for the child to sit the same way even when the need for it does not exist.

Disuse is an occasion under which some function or functions of an organization are held in abeyance. During this time a new equilibrium is established by the remaining active functions. These functions or new ones unfamiliar to the original organization may, under the changed conditions, produce results which are unfavorable to the return of the part later to its original form. In this way, where a limb is kept at rest too long serious circulatory, nutritional, and tissue changes occur that result in degeneration and atrophy of essential structures.

Conditions of this kind exist in the operation of many factors which interfere with normal posture. To mention one, the tendo-Achilles shortens under the limited excursions brought about by the constant use of high heeled shoes. This is partial disuse but the consequences are at least disabling.

Since disuse is only an occasion under which active processes proceed without the absent functions it cannot be considered as a

categorical etiologic factor. It is like time; it causes nothing but permits much.

The Effects of Faulty Posture.—Whenever one organization exerts an influence on another the forces concerned effect some changes in the functions of both. These changes may be insignificant or highly important depending on the degree of inter-dependence of the functions.

Faulty posture is a disturbance of relationship between parts (organizations) and must always be accompanied by changes in their force relationships as well. Thus, when the shape of the thoracic cage is altered by bad posture, all structures intimately related to it must undergo some shift in their equilibrium, which involves their functions to some degree.

On the principle that every organization is built up of lesser organizations and that each level or organization possesses functions peculiar to itself it is logically demonstrable that any disturbance of one function must have an effect on all functions. But certain of these functions may be so far removed from each other that the changes occurring in one as a result of change in the other may be so insignificant as to be practically immeasurable. That point of separation of functions at which effects become insignificant has been called the point (or zone) of "virtual indifference."[1]

It is this point of virtual indifference which must be determined in the study of the effects of faulty posture. For example: The functions of the kidney are practically indifferent to vascular changes brought about by faulty mechanics in an arm whereas there is an intimate relationship between the vascular structures in the pedicle of the kidney and the functions of the kidney so that any mechanical process which influences the pedicle to a harmful extent may alter some functions of the kidney.

The problem of the relationship between form and function is of the same nature. The form of an organization (cell, tissue, organ, or the entire body) is an expression of its functions. Its size and shape is determined by and determines the limitations of its inferior functions. Any change of form must influence all levels of organization but will affect some more significantly than others. Thus, constriction of the lung by a compressed thorax may materially reduce its vital capacity but will interfere to an insignificant degree with the processes of gaseous exchange.

When the principle of virtual indifference is combined with that of the limit of tolerance in physiologic equilibria it becomes apparent that it is difficult to be certain of dogmatic statements made on the effects of faulty posture. Out of the wealth of material which has been written on this subject there are very few clearly demonstrable

[1] Friend, J. W.: Unpublished Lectures on Logic, New Orleans, 1930

facts and fewer still which can be predicted or measured. In this review no attempt will be made to cite all instances of disturbed function arising from faulty posture. The present concern is only with the principles involved, so that but a few of the better understood effects will be given to illuminate the text.

While it is difficult to measure the relative importance of bad habits and poor nutrition in the development of faulty posture there is little doubt that some mechanical defects and functional derangements result from the bad posture itself aside from the action of these two primarily effective causes. A young adult with a postural scoliosis of long duration may exhibit secondary changes in the pelvis and lower extremities as the result of mechanical compensation. Tilting of the pelvis and apparent shortening of one leg can in turn lead to further mechanical defects in other parts with muscle imbalance, increased fatigability and a long train of associated symptoms and functional inefficiencies. When such bad dynamics involves the muscular and fascial walls of the abdominal cavity some of the essential forces which aid in the support of abdominal viscera are altered to a degree which permits the viscera to assume new positions in the equilibrium. Prolapse of individual organs may develop or there may be a general visceroptosis. When other factors such as trauma of childbirth, hereditary or congenital weakness of muscle and fascia arrangements, tractions caused by increase in weight of organs, etc., are present in addition to faulty dynamics of postural origin, the likelihood of visceral displacement is greatly increased.

The alleged relationship between poor chest expansion and the development of pulmonary tuberculosis is an illustration of the difficulty of proving the influence of faulty posture as a causal agent of disease. The cramped and twisted thorax certainly expands less effectively than the normal chest. As a result it is concluded that there is less relative movement of the apical lungs and a corresponding diminution in the circulatory efficiency and aëration of these parts. The proponents of the postural theory then jump from this anatomic-physiologic observation to the conclusion that it favors the development of tuberculous processes. It is hardly necessary to point out that this leaves a gap between cause and effect which has been bridged by only the most meager information.

Carnett has repeatedly stressed the importance of poor body mechanics in the production of subjective somatic disturbances. The following quotation is from this observer's discussion on body mechanics at the White House Conference on Child Health.[1] "After prolonged study of the problem of so-called operative failures, I

[1] Carnett, J. B.: Discussion in "Body Mechanics: Education and Practice," Committee on Medical Care for Children, White House Conference, New York, Century Company, 1932.

came to the realization that in the great majority of patients complaining of abdominal pain and tenderness, these symptoms are located in the abdomen. Further studies disclosed that the usual cause of pain and tenderness in the abdominal wall is an irritation of the spinal nerves where they make their exits through the vertebræ and that the commonest cause of this nerve irritation is bad body mechanics, and further that even partial correction of bad body mechanics cures the abdominal pain and tenderness."

The influence of faulty posture (and nutrition) on the general wellbeing of school children has been best brought out by the Chelsea Survey.[1] *In their conclusions on this survey, Klein and Thomas* state that "improvement in body mechanics was associated with improvement in health and efficiency. Improvement in posture was found to occur more frequently with training if there was improvement in nutrition as well. Among the children without posture training, improvement in posture occurred more frequently with those in the best nutritional condition. Training was the most essential factor in the acquisition of good body mechanics, and good body mechanics was associated in a small proportion of the children with improved nutrition. Since nutrition has been accepted as an important index of a child's health, posture training would seem to be an important factor favorable to health, as indicated by its association with improved nutrition." More specific conclusions are "The result of the practice (of habitual and steady retraction of the lower abdominal wall) is the elevation of the stomach, intestines, and other abdominal organs. Posture training is therefore, a safeguard against visceroptosis, which is frequently associated with poor health." "Posture training improved the tone of the abdominal muscles and reduced the fat deposited in the abdominal wall." "About four-fifths of the children observed had pronated feet. This condition was most frequently associated with poor body mechanics. It was more frequent among children of the thin type and was less among children with good nutrition." "Postural, habitual or functional lateral curvature of the spine (scoliosis) disappeared generally with improvement in body mechanics." "Posture training and the maintenance of correct posture contributed to the health and efficiency of normal school grade children."

Non-postural Stresses.—While the mechanics of posture may exert forces on organ arrangements which are not directly concerned with normal posture and disturbances of organ relationships may be factors in faulty posture there remain many forms of internal stress which under certain circumstances become excessive or diminished to the point of producing harmful effects. These manifestations are processes which have their own causative factors and

[1] Klein, A., and Thomas, L. C.: Posture and Physical Fitness, Children's Bureau Publ. No. 205, Govt. Printing Office, 1931.

the abnormal dynamic forces only arise in them as a result of antecedent categorical causes. *If an enlarged liver produces dynamic* changes in the structures in relationship to it the cause of these changes must not be sought in the enlarged liver but in the causes of the enlarged liver.

On the whole it is the non-postural stresses which make up most of the dynamics of the body. When the body is in its most favorable postural equilibrium the internal stresses continue to act. Even when it is almost completely relaxed in sleep the forces of respiration, circulation, movements of viscera, muscle tone, and *pressures and tensions between parts go on. If any of these are of* sufficient strength or character to influence other structures or functions harmfully they may give rise to disease.

A few examples of non-postural dynamic influences are given below to illustrate the manner in which they operate as mediating causes.

Among the hydrodynamic systems of the body are those in which *increased or decreased pressures act to propagate or deflect the* forces into a more serious series of consequences. Under normal conditions the brain and its contents are in equilibrium with the pressure forces of the cerebrospinal fluid. When for any reason a blockage occurs in the mechanisms for removing the fluid from the subdural spaces or ventricles the cerebrospinal fluid pressure rises and exerts effects on the yielding brain which may be more serious than the primary effect which caused the blockage. In the same way a mild iridocyclitis may through chance of location involve the drainage area of the eye and set up an entirely new system of force by increasing intraocular pressure.

The altered dynamics of a leaking aortic valve result in secondary mechanical alterations of vital organs which may end in death of the patient. Hydroperitoneum from cirrhosis interferes seriously with diaphragm excursion which in turn influences venous return and embarrasses heart action.

Abnormal pressures from gases may also cause untoward effects beyond what might have been anticipated from the antecedent factors. The rupture of an emphysematous bleb beneath the visceral pleura causes pneumothorax which if made persistent by a valve-like action at the rupture may reach a pressure within the pleural cavity of a degree that will do much more harm than simple collapse of the lung. An opening from the trachea or larynx through a rupture which permits the atmospheric air to enter the subcutaneous tissue may result in a generalized subcutaneous emphysema with serious consequences. Gaseous distention of the stomach and intestines is dangerous when the walls of these organs have been previously weakened.

Although many factors predispose to the development of inguinal and other hernias, dynamic pressures play an important rôle in

their natural history. The repeated accentuations of intra-abdominal pressure brought about by coughing, bending, straining at stool, and weight-lifting cause the mobile, air-water containing intestines to bombard the weakened abdominal wall. At some moment when the gut has insinuated itself into the area of lessened resistance, a sudden increase in pressure may force it the rest of *the way and the potential hernia becomes manifest.*

Obstruction of the external auditory canal or Eustachian tube disturbs the air equilibrium on both sides of the tympanum and *interferes mechanically with the transmission of sound waves; a* vacuum may develop in the sinuses of the nose by one way blocking of the exit of air; air emboli in the circulation block the flow of blood through small vessels as effectively as solid particles; bronchial obstruction may produce atelectasis or emphysema in the lung beyond.

The size and mass of an organ can be increased by overgrowth or hyperplasia, new growth, engorgement, accumulation of secretions, inflammation and many other pathologic processes. Such increase always means encroachment on other structures and the establishment of new dynamic relations between them. The latter may be of the nature of a push or pull and so dislodge the neighboring organs. For example, a large, heavy diseased testicle may exert tension on the cord and favor the development of hernia; *masses of different kinds can exert pressure on nearby vessels and* cause local anemia of other tissues by obstruction of the arterial blood supply or stasis by obstruction to veins; an enlarged displaced *uterus may not only interfere with its own functions but exert* untoward influences on the bladder and rectum.

Non-postural muscle and bone defects of structural or functional nature can likewise disturb the static equilibrium of parts not involved in mechanical movement. When these tissues act as containers or supports for other organs or tissues, derangements in them can produce side effects not a part of the original disease. Such are seen in Paget's disease of the skull, tumors, degeneration, atrophy and softening of bone, paralysis of muscles such as those of the diaphragm, stomach, intestines, any of the sphincters, soft palate, esophagus, abdominal wall, levators of the pelvis and the extrinsic and intrinsic muscles of the eye. Diseases of muscles other than those resulting in paralysis may also disturb their mechanical relation with other parts.

This review emphasizes the important rôle of static mechanical force in the natural history of many of the most common diseases. It must be reiterated that these are not primary initiating factors *but segments of events which have been inaugurated by other* causes. They in themselves do not explain disease but only aid in describing it.

EXTERNAL MECHANICAL FORCE.

Mechanical forces which originate in the environment exert their effect by adding new stresses to body mechanisms, opposing accustomed resistances, and disorganizing cell, tissue and organ integrity. In their ultimate analysis each of these effects is a disturbance of equilibrium brought about by the conversion of the external force into a component of the forces within the organization which they affect. Unless this occurs the force is ineffectual.

In this, as in all other phenomena which exhibit tendencies to disturb the organization of living material, the force must be of such strength and nature as to disturb physiologic equilibria beyond their point of tolerance. Thus a mild pressure applied for a short time may temporarily distort the physical structure of a part, or interfere with its circulation, without forcing any of its functions beyond the point where they can restore themselves by the use of their normal accustomed mechanisms. This pressure may cause pain, and produce anemia and tissue anoxemia with temporary failure of other functions but the entire organization can return to its original state by its own powers after the pressure is released. If a small vessel is ruptured however, or a nerve ending injured or the continuity of the skin broken, reparative processes must intercede to restore the part to normal. Under the latter circumstances pathology has resulted; it is observable and measurable whether it lasts for a long or short time, and it is identified by the appearance in the organization of functions potentially present but not ordinarily present in that kind and degree in the normal processes of the functions concerned.

Every contusion, sprain, fracture, and stretching injury shows its effects by adding new stresses to body mechanisms. The effective causes in these instances exert force against resisting structures and meet with more or less success in disarranging structure and disturbing function.

The opposition to accustomed resistances is exemplified by the removal of the opposing action of muscle groups through prolonged immobilization by splints, forceful restriction to movement by tight corsets, garters, ill-fitting shoes and orthopædic appliances or the sudden release of accustomed resistance shown by the adjustments necessitated through the loss of teeth or any other bodies whose functions depend on normally opposing forces. The apparent negativity of this type of mechanical force is due to the masking of the antecedent force by the changes it produces. Some of the effects may be attributed to secondary changes induced by the altered body dynamics as indicated in the previous section. The processes of disuse are also created by this loss or diminution of opposing forces. Neither of these two processes must be confused with their cause.

Disorganization of the integrity of structure is shown in all lacerations, *tears, abrasions, puncture wounds, fractures, ruptures,* crushings, and severe concussions. In them the force must be sufficient to cause the separation of contiguous structures or parts of *structures whether this separation be molecular as in concussion of* the brain or gross as in the vast number of traumatisms where dissolution of continuity occurs.

It is obvious from these examples that this force is responsible for most of the common traumatisms and accidents of daily life. Its source therefore is potentially present throughout the physical environment and its effect is felt either by intercepting it while in motion, resisting it when it is static, or meeting with its resistance when the parts themselves are in motion.

THE DEFENSES OF THE BODY AGAINST EXTERNAL MECHANICAL FORCE.

The resistances of a physical body against mechanical force are measured by its resilience, elasticity, stretch, and crushing strength. Its total resistance is further modified by the conditions under which the body is disposed when the force acts, that is whether it is free to move under the force or is restrained by its surroundings.

In the human body these all play their part to varying degrees. Thus, resilience is more evident in muscle than in bone but less than in skin; elasticity is greater in bone than in cartilage; crushing strength is greater in teeth than in bone; there is more freedom of movement between the bones of the extremities than the bones of the skull and the brain is less able to give way to a compressing force than the abdominal viscera. The mobility of joints permits the levers of the extremities to move and absorb without damage many forces which might otherwise fracture the bones; the resilience of the abdominal wall and the dynamics of its contents allow considerable pressures without danger of rupture; the flexibility of the skin and its ability to move over the loose connective tissue beneath protect it from tearing and splitting forces; bumpers and dampeners made of fat, cartilage, connective tissue, and fluid take up most of the ordinary shocks to which the body is constantly exposed.

All of these mechanisms add to the margin of safety against damaging disturbances. Due to changing muscle tonus and the variable rigidity of muscles under reflex or voluntary contraction the body is never in a constant state of ability to defend itself against outside forces. There are occasions when muscle relaxation is a more effective defense than muscle contraction. Thus, a muscle fracture of the patella cannot occur if the extensors of the knee are completely relaxed when the foot is suddenly arrested by tripping. The common saying that a drunken man is less liable to injury from a fall is based on the fact that he is relaxed and does not tense

his muscles to protect himself. Rigidity diminishes the opportunity for the arms and legs to flex or extend under the force.

On the other hand tense hard muscles are more effective in distributing and absorbing the force of blows. Shock is less likely to follow a blow on a hard abdomen than one which is soft, fatty and relaxed. Compression of the chest is better resisted by a strong musculature.

The important viscera, blood-vessels and nerves are deep-set within protecting coverings and are permitted considerable freedom of motion. When normal they can be damaged only by inordinately excessive external mechanical factors; for penetrating instruments to reach them the resistances and tendencies to deflection by the numerous overlying layers must first be overcome. In many of these organs a considerable part of the covering is bone.

CHAPTER XXVIII.

THE DEFENSE AGAINST MECHANICAL FORCE.

PREVENTION OF FAULTY BODY DYNAMICS.

Poor Posture.—Given a body normally developed without obvious asymmetries, the most effective means to prevent faulty body posture will be the inculcation of good habits of sitting and standing and the maintenance of a good state of nutrition. The first is especially necessary in the face of improper seating and desk arrangements which favor faulty attitudes in the school and home. It is generally taken for granted that a child seated at a poorly designed school desk must acquire poor sitting posture. This can be agreed with when other predisposing factors are present but a healthy, well nourished, happy child is not quite so susceptible to faulty molding. It is the disinterested, slumping child who not occasionally, but always, slouches, who is liable to become a victim of fixed habits of sitting and standing. Training, mimicry, emulation of the upright form in others are more powerful determiners of good posture than the physical arrangements are to poor attitudes. The disadvantages of bad seat and desk arrangements are centered largely around their fatigue producing effects. When a child has to double his legs under him to raise his body to a comfortable height for his desk he fatigues rapidly and cannot maintain that position. The same is true when he must sit on the edge of the chair to reach the desk set too far in front of him. Fatigue does not limit itself to the muscles immediately concerned but involves the whole body and induces a general slump. On the other hand it cannot be said that the healthy normal child will always sit well on the carefully planned, physiologically perfect posture chair at a desk as thoughtfully provided to fit his individual needs.

It is when the other important factors of nutrition and psychic interest are at low ebb that poor physical seating arrangements encourage the unphysiologic imbalances of faulty posture. Such a child sits poorly, stands poorly and in general, moves poorly.

Too long hours at a single task are fatiguing to the active child. School periods should be so staggered with recess, lunch time, and changes of interest that neither muscular, psychic or general body fatigue have time to develop beyond minimum amounts.

Attention to defective hearing and vision is necessary to remove the need for strained positions which favor these faulty mechanisms.

rugs on polished floors, falling down from rocking chairs and so forth, but there is little excuse for failing to take a little precaution and to use common sense. Few of these accidents are beyond control by the simple expediency of using a little more care and thinking just a little ahead of the immediate present. It is the principle in "look before you leap."

The same applies to the use of tools and the handling of machines. Assuming that the individual is of sufficient age and intelligence to use mechanical appliances it does not necessarily follow that he will not injure himself in their use. Many automobile accidents result from failure to fix the attention on the needs of the moment and exercise a modicum of forethought against possible eventualities. The most skilful technician may suffer injury from the machine he knows best if he permits himself to become careless.

Accidents due to mechanical failures can be avoided in part by careful construction, frequent inspection, and early repair of mechanical parts. It is the rickety ladder, worn brakes on motor vehicles, unsafe scaffolding, broken boards on floors, loose parts in machinery, and use of faulty material in construction that account for many accidents.

When any individual factors are present, such as sickness (either physical or mental), exhaustion and fatigue, or defects of body mechanics, the need for attentiveness and forethought become doubly necessary.

It must be admitted that many unpredictable and unexpected hazards exist which make life dangerous under many circumstances. One can hardly be expected to anticipate at all times, for example the possibility of injury by falling bodies, explosions, motor cars out of control, attack by men and animals, or collapse of buildings and other structures. But there remains a little hope of avoiding some degree of injury in even these by quick and effective responsiveness of mind and body. There are some who respond so rapidly to awareness of danger that they appear to escape injury almost miraculously. There can be little doubt that some of this ability may be bettered by training.

Because of the wide variation in individuals and the probability that some one will be hurt at some time by certain factors in the environment the principle of safety first has been quite generally adopted. Whenever known hazards exist protective devices should be employed Guard rails on bridges, railways, and dangerous roads; screens and rails around machinery; reduction in movable parts of machinery or coverings to make them inaccessible; fenders on moving vehicles; safe treads on stairs; carpets nailed down or weighted on slippery floors; non-skid devices of all kinds, represent but a few such devices. The person may be protected further from mechanical injury by the use of goggles, gloves, headguards, specially

designed clothing, such as heavy boots, leather vests, and aprons, finger cots, thimbles, etc. Unfortunately, many of these are uncomfortable and cumbersome and workers would rather take a chance than use them.

Certain general measures have helped to reduce the possibility of accidents. Governmental measures which aim to place *liability* for accidents on employers have forced many manufacturers to the use of protective devices. The compensation laws have made it worth while in dollars and cents to prevent accidents to employees; *trade unions have insisted in some instances that their members cannot* work under certain unsafe conditions; public opinion and the use of the tax payer's money have brought pressure on civic organizations to build safe roads and bridges.

Government inspection in public works aims to prevent accidents by assuring the use of reliable material and the erection of safe buildings. Insurance companies and underwriters require that the operations which they cover meet certain specifications as to structure, *material and margins of safety.*

Although motor vehicle regulations are still in their constructive stage they have the potential power to prevent many accidents by such measures as examination and licensing of drivers, brake test *certificates, traffic control, and deterrents to careless driving.*

In conclusion, accidents happen because of knowable causes. They originate from definite circumstances in the environment and affect the individual through mechanical force operating in a particular way to a particular degree. The *application of the principle* of intervention in the prevention of injury by external mechanical force must logically succeed by just that amount to which it can be effectively employed. Nowhere near the limit has yet been reached in the effort to prevent preventable accidents. In the long run education will be the main factor for it creates awareness of danger to the individual and to others and reveals the need for all preventive measures which can possibly be applied.

CHAPTER XXIX.

THE INFLUENCE OF BAROMETRIC PRESSURE.

The atmosphere exerts a pressure of 14.7 pounds per square inch at sea-level. By the laws of gases this pressure is equal in all directions and is transmitted to all sides of all objects to which it has access. But even at sea-level this pressure can be varied by the action of other forces which are not in equilibrium with it. Thus atmospheric pressure can be raised to a barometric pressure greater than 14.7 pounds per square inch by compression of air in a closed chamber or the barometric pressure reading can be brought lower than atmospheric pressure by the creation of a partial vacuum. Most measuring devices register the amount of change above or below atmospheric pressure. When condensed air is measured at 15 pounds it means that it is atmospheric pressure (14.7 pounds) plus 15 pounds, or 29.7 pounds. This measurement, being 29.7 pounds above actual zero pressure is called the absolute pressure. If the measurement is exactly twice 14.7 or three times 14.7 it is spoken of as 2 or 3 atmospheres respectively. Should the instrument be calibrated to read zero at atmospheric pressure then in the example cited the readings would be plus 1 and plus 2 atmospheres. A force of 14.7 pounds per square inch is able to sustain a column of water 33.9 feet high. If the water is contained in a tube 40 feet high the water cannot be forced above 33.9 feet by atmospheric pressure alone even though there be a vacuum in the 6-foot space allowed for it. Nor can it be drawn above the 33.9 foot mark by suction.

This principle is employed in the liquid barometer but because of the bulk and unwieldiness of an instrument 34 feet high mercury is substituted for water. Since mercury is 13.6 times heavier than water it can be supported in a column only 29.9 inches high (1/13.6 of 33.9 feet). This is often expressed as 760 mm. of mercury.

Under stable atmospheric conditions at sea-level the entire external surface of the body is subjected to a pressure of 14.7 pounds per square inch. Within the body the same pressure exists in every part to which air has free access. In partially closed chambers which are subject to kinetic pressure changes the barometric pressure will register somewhat above or below 14.7 pounds depending on whether the kinetic forces result in compression or exhaustion of air. In the lung at rest the intra-alveolar pressure is 760 mm. minus the elastic pull of the lung tissue; during rapid expiration it is raised slightly above 760 mm. by compression of

short, quick duration; the normal pressure on the two sides of the membrana tympani is equal at 760 mm. but it may be increased or decreased on either side by obstruction of the Eustachian tube or external auditory canal.

From the moment of rupture of the amniotic membranes at birth the human infant becomes subjected to atmospheric pressure in place of the hydrodynamic forces of the amniotic fluid. The physiologic readjustments to the changed conditions are rapid and permanent. The chest wall expands, the lungs fill with air, the respiratory cycle is initiated, air enters the alimentary tract, and all parts of the body come into stable equilibrium against the pressure of 760 mm. of mercury. From this time on further physiologic adjustments are necessitated only by shifts in the external atmospheric pressure. Such shifts may result from natural or artificial causes and can take place slowly or rapidly. The effect on the physiologic equilibria will therefore vary with the rate and degree of change.

At any given altitude the barometric pressure varies slightly with the passage of areas of high and low pressures brought about by meteorologic conditions. The studies on mass air movements, cyclonic storms, air movements due to local and general temperature changes, ionization of air, and other meteorologic factors, show that barometric pressure varies with these conditions but that the change is limited to a relatively small range of a few inches. A high barometric pressure due to any of these causes would be in the neighborhood of 30.5 inches of mercury and a reading as low as 29.0 inches is exceptional.

There has been much speculation on the possible effects of these small pressure changes on man in health and disease but little of it bears the brand of scientific accuracy. Man has long observed the exacerbation of rheumatic symptoms in anticipation of the onset of storms and changing weather conditions but such correlation, acceptable as it may be, does not prove a causative relationship. The behavior of birds and animals before approaching storms is given as corroborative evidence. None of these observations can point to the meteorologic factors most involved in explanation of the phenomenon. That it is due to barmometric change alone is only surmise.

Smith[1] has demonstrated that there is water retention in the bodies of dogs and rats when the barometric pressure is lowered 2.6 cm. to 9.8 cm. of mercury during a period of twelve to forty-eight hours and that this disturbance of water balance is accompanied by restlessness. He concluded that possibly hydration is the mechanism which induces reactions in many animals and some people to changing weather.

[1] Smith, C. S.: Am. Jour. Physiol., 87, 200, 1928.

More marked changes of barometric pressure occur on the ascent to higher altitudes or descent below sea-level and submersion in deep water.

Atmospheric pressure diminishes at the rate of approximately 1 inch of mercury for every 1000-foot gain in altitude. The factor of greatest physiologic importance accompanying this decrease in atmospheric pressure is the alveolar oxygen tension (per cent of oxygen x absolute atmospheric pressure in millimeters of mercury). Reduction of oxygen tension results primarily in the production of anoxemia. Although most people will be affected by this at altitudes of 3000 to 5000 feet if the ascent is rapid, individual differences do not appear until the 7000 to 10,000 foot mark is reached.

Altitude or mountain sickness (airplane sickness) is characterized by dizziness, torpor, malaise, and anorexia. It may be so troublesome as to bring on actual vomiting. The work output is diminished and fatigue occurs early. At extreme heights (20,000 feet) the labor of climbing is so severe that only a few steps can be taken before rest becomes acutely necessary. These symptoms are primarily due to air hunger in the tissues brought about by oxygen want.

Grollman[1] made careful studies on the metabolism of individuals who ascended to an altitude of 10,700 feet (Pikes Peak) after having first been acclimated at sea-level. His conclusions were that the cardiac output of young normal individuals at this altitude is gradually increased during the first few days after their arrival from a low altitude but that it soon begins to decline and resumes its normal sea-level value within two weeks. The cardiac output was found to increase as much as 40 per cent in five days. He does not believe that the decreased oxygen tension acts as a direct stimulus to the cardiac output.

Grollman further observed that soon after arrival at the high altitude the hematopoietic system is stimulated. Du Bois[2] found an increase of reticulated red blood cells at this same altitude (456 mm. of Hg., Bar. Press) and a hemoglobin count as high as 122. In the ascent of Pikes Peak, Du Bois found a rise of 10 per cent hemoglobin for every 100 mm. drop in pressure after reaching the 7000 foot level.

These observers and others conclude that in acclimatization to high altitudes the increased hemoglobin content substitutes for the increased cardiac output and permits the latter to restore itself to its sea-level value.

Du Bois found no significant change in the basal metabolic rate at 10,000 feet, a slight shift in the pH of the blood toward the alkaline side, diminished ammonia formation by the body and increased excretion of alkali by the kidneys. He found that complete compensation for this alkalosis never occurred.

[1] Grollman, A.: Am. Jour. Physiol, 93, 19, 1930.
[2] Du Bois, E U. S. Nav. Med Bull, 26, 833, 1928.

Peterson[1] studied the influence of low atmospheric pressure on the leukocytes and demonstrated that it produces a relative lymphocytosis with a decrease of 10 to 14 per cent of the polymorphonuclear leukocytes. The leukocytosis in 13 out of 100 individuals examined was above the usually accepted upper normal limit of 10,000 per cu.mm.

Cook[2] has given striking evidence that the effect of high altitudes is not alone due to simple reduction of oxygen tension but that the reduced total pressure *per se* is of importance. Cook tried, in his own words, "to see if the old assumption were true that the effect of a reduced oxygen tension, whether secured by reducing the percentage of oxygen at atmospheric pressure or by reducing the total pressure (effect of altitude) would be the same." He concludes that the different action of reduced oxygen tension and reduced total pressure was not wholly due to purely physical causes having to do with solution and diffusion of gases, but is dependent on the organization of the cell itself. To explain this he assumes the existence of a cell catalyst which is concerned only with the *uptake* of oxygen in the cell and not with its whole oxidation processes.

The upper limits of physiologic adaptation to high altitudes for man is set by Campbell[3] at 18,000 to 20,000 feet. At this elevation the oxygen has dropped to 10 per cent and although he points out that Thibetans, yaks and other animals can survive at this height for several months it is not reasonable to speak of this as true acclimatization. Under 10 per cent oxygen and over 20,000 feet he considers it pathologic, not physiologic adaptation. Haldane places the physiologic limit on the basis of water vapor pressure in the lungs. At body temperature this pressure is always 47 mm. of mercury no matter what the altitude. If the barometric pressure were to be reduced to 47 mm. the lungs would be entirely filled with water vapor and cause asphyxia. It is the water vapor which becomes the limiting factor according to Haldane when an aviator goes much higher than 30,000 feet.

Barometric pressure increases so slowly with descent in air below sea-level that within the distances penetrated by man this increase is practically negligible.

He is artificially subjected to high pressures, however, under certain conditions where the air pressure is raised within closed chambers for the purpose of giving support against high external pressures. This is met with in subterranean construction work and in working at deep water levels. Unprotected divers are also subjected to pressures greater than the atmosphere due to the pressure of the surrounding water.

Men employed in occupations necessitating compressed air

[1] Peterson, R F, and Peterson, W. G. Jour. Lab. and Clin. Med, 20, 723, 1935.
[2] Cook, S. F.: Jour. Gen Physiol., 14, 55, 1930.
[3] Campbell, J. A.: Brit. Jour Exper. Path, 16, 39, 1935.

chambers work under pressures of 2 to 5 atmospheres and deep-sea divers going to depths of 180 to 200 feet are subjected to 6 to 10 atmospheres.

At these high pressures it is the partial pressures of the gases and not their percentage which is of physiologic significance. Under working conditions the percentage of oxygen is maintained by air movements and intake of fresh air.

The outstanding influence of high pressures on man is the altered nitrogen balance in the tissues. Du Bois[1] expresses the problem concisely as follows: "In round figures the blood at sea-level contains 1 per cent nitrogen gas in solution and most of the tissues are supposed to be in equilibrium at this level. Under increased pressure it takes several hours (three hours according to Haldane) before the blood can transport from the lungs enough nitrogen to saturate the whole body at the new pressure. Those parts whose circulation is good, such as the muscles, glands, and brain, saturate more rapidly than the ligaments, bones, and white matter of the cord. The fat depots with their high affinity for nitrogen and very scant vascular supply will not be fully saturated for a long time."

According to Cunningham[2] the nitrogen tension in the spinal fluid varies nearly directly with the barometric pressure. Thus at 5 atmospheres (absolute) the nitrogen content of the cerebrospinal fluid is 5 times that at sea-level pressure.

When a man who has been subjected to high pressure for a sufficient length of time to permit saturation of his tissues with nitrogen under the new tension, is suddenly released from this pressure, the nitrogen in solution "froths" and forms bubbles in the tissues. That is, it cannot be removed quickly enough by the circulation and the lungs before the pressure is reduced to the point where the nitrogen will pass out of solution and form bubbles. Those parts where the circulation is poorest and affinity for nitrogen greatest will give up nitrogen last and thereby be subject to gas formation at pressures a little above one atmosphere. The white matter of the cord has a little less affinity and slightly more vascularity than fat tissues and might be able to free itself of excess nitrogen before sea-level pressure is reached. But if decompression is too rapid bubbles of nitrogen form in the spinal cord and produce serious damage. These bubbles in nerve, blood and other tissues may act as emboli, produce local pressure symptoms, and if large enough, cause actual physical damage.

The symptoms accompanying this process produce the classical picture of the "bends" or caisson disease. In some instances the symptoms may be delayed for several hours after decompression

[1] Du Bois, E. U. S Nav. Med. Bull, 27, 311, 1929.

[2] Cunningham, O. J, Rand, J. H., and Weckesser, E C. Am. Jour. Physiol., 107, 164, 1934.

apparently due to gas bubbles forming originally in innocuous areas moving later to other parts where they produce symptoms.

Slow decompression gives time for readjustment of the nitrogen concentration and allows the gas in the tissues to be taken up by the blood and eliminated through the lungs. A succession of such readjustments permits the nitrogen tension to diminish coincidentally with alveolar air tension and so prevent the disproportion which results in bubble formation. This is accomplished by the use of air locks with successively lower air pressures. The workman passes through them in succession; first through the lock with a pressure lower than that under which he has been working, and last through one with a pressure a little above one atmosphere.

Exclusive of the pathologic physiology responsible for the "bends" the increased partial pressure of the nitrogen is responsible, according to Behnke[1] and his coworkers, for other symptoms in the worker under high barometric pressures. These observers state that high barometric pressures have a narcotic effect on man which first makes its appearance at 3 atmospheres. This effect is characterized by slow mentality, and impaired neuromuscular coördination. At 4 atmospheres there is increased liability for making mistakes, past-pointing and exaggerated movements. These are accompanied by a sense of well-being. At 10 atmospheres judgment is impaired, there is difficulty in assimilating facts and making quick decisions. Sensory reception is not affected but there is delayed response to sensory stimuli. Stupefaction can occur at this high pressure. They infer that the physical properties of nitrogen render it analogous to narcotic substances due to its high coefficient of solubility in lipoid matter.

Stott[2] reviews a number of predisposing factors which he believes are responsible for the individual differences seen in those subjected to similar pressures but only some of whom develop caisson disease.

Personal equation factors:
- Efficiency of circulation.
- Debilitation from disease.
- Malnutrition.
- Alcoholic excess.
- Constipation.
- Chronic fatigue.
- Effects of cold and exercise.

Organ disease:
- Arteriosclerosis.
- Heart lesions.
- Respiratory disease.
- Anemia.
- Edema.
- Status lymphaticus.

Age: Rate increases over thirty years. Those over forty with few exceptions, are excluded from work under high pressures.

Obesity: Fat men are ill-fitted. Fat prevents rapid desaturation.

Fatigue: Impairs circulation.

[1] Behnke, A. R., Thomson, R. M., and Motley, E. P.: Am. Jour. Physiol., **112**, 554, 1935

[2] Stott, A. A.: Indust. Med., 3, 43, 1934.

CHAPTER XXX.

THE EFFECTS OF COLD AND HEAT.

The cells of the body of man are adapted to a temperature range of about 95.8° F. (53.2° C.). The extremes are approximately 21.2° F. (−6° C.) and 117° F. (47.2° C.). The former is the limit set by the freezing-point of protoplasm and the latter is the point at which the proteins begin to coagulate.

The organization of man as a whole can stand a much wider variation of external temperatures because of protecting and adjusting mechanisms which prevent the body cells from reaching these extremes. The length of time over which the body is exposed is of importance. The adjusting mechanisms are efficient enough to enable a man to survive an external temperature of 248° F. (120° C.) for a few minutes, but if the body temperature reaches 108° F. (42° C.) and is permitted to remain at even this low temperature for more than two hours the proteins of some cells will begin to coagulate. It is for this reason that 108° F. is considered as a critical height for sustained fevers. At the cold end of his temperature range man can withstand temperatures as low as −40° F. (−40° C.) to −60° F. (−51.1° C.) provided he can keep active and is not exposed for long. Reincke[1] reports the recovery of a drunken man who had been exposed to cold and showed a rectal temperature of 75.2° F. (24° C.).

The body as a whole reacts to a limited degree to changes in environmental temperature in the same manner as inanimate physical bodies by absorption and elimination of heat. Various investigators have shown temperature gradients at distances beneath the skin surface which are independent of temperature changes due to vascularity and other processes that might affect it.

Unless the temperatures are extreme the purely physical changes are of negligible physiologic importance. When they do assume an important rôle it is generally under circumstances in which the heat or cold is applied to local parts and acts locally.

Changes in body temperature due to environmental heat and cold are the result therefore of a complex of physical exchange, physicochemical change, and general adaptive mechanisms. Since the body is a heated body the temperature of which is maintained by an adjustable heat mechanism, its reaction to temperature influences is dynamic. It is a positive adjustment, most marked when the

[1] Reincke, J. J.: Deutsch. Arch. f. klin. Med., 16, 12, 1875

entire mechanism of the body is involved, less so in the case of local tissue reactions, and quite limited when individual cells only are affected. In each of these processes there is a limit of tolerance, as has been indicated in the discussion of the temperature ranges of the cells and body at the opening of this chapter.

Cold.—Cell tolerance to low temperature is efficient until the effects of freezing become manifest. This point varies with different cells and depends on their water content and probably also the relative proportion between their free and bound water. Cells with small amounts of water can withstand freezing and subsequent thawing without apparent damage. Although cell metabolism is slowed almost to a standstill and mitosis is reduced they may be revived by restoring them to their natural temperature. Brooks[1] states that a temperature considerably below −20° C. (−4° F.) (roughly between −40° C. (−40° F.) and −60° C. (−76° F.)) is required to freeze the free water in muscle completely. Wells[2] remarks that the effects of freezing on cells is physical and results from the current set up about the ice crystals in thawing, the concentration of the cell constituents which results from the freezing-out of water, and the rapid contraction and expansion under the influence of the cold and ice formation.

These effects are described by Aschoff[3] as a depression of the speed of chemical reactions, disturbance of colloid and intercellular substance exchange, changes in osmotic pressure on account of the presence of salt-free water, gel formation, vacuolization, shrinking of the nucleus, and general injury to cell vitality with eventual disintegration and necrosis.

Local tissue reactions to cold depend on the disturbed equilibrium brought about by the above cellular changes, alterations in the physico-chemical state of the tissue fluids and electrolytes, changes in the temperature of the blood, increased permeability of cell walls and capillaries, liberation of the products of deranged cell metabolism, and the effects on the nerve elements in the tissue.

The local tissue effects of cold are seen in occupations in which refrigerants are handled, as in cold storage plants, in occupations requiring submersion of the hands or feet in cold water such as in digging ditches and drains in the open, longshore work, road work, marine labor, hunting and trapping, plumbing, and excavating. Cold air may freeze or nearly freeze exposed parts such as the fingers, tip of the nose, and external ear under any conditions of labor, outdoor sports, or accidental exposure where the individual is subjected to cold for a long time. Contact with extremely cold objects may be met with in ice-handlers, packers of dry ice (solid

[1] Brooks, J.: Jour. Gen. Physiol., 17, 783, 1934

[2] Wells, H. G.: Chemical Pathology, Philadelphia, W. B. Saunders Company, 1925.

[3] Aschoff, L.: *Pathologische Anatomie*, Jena, 1923.

carbon dioxide), and in those foolish enough to try the precarious experiments of touching the tongue to cold metal or placing dry ice in the mouth. Deliberate local freezing is seen in the use of ethyl chloride spray for anesthetic purposes and the therapeutic application of carbon dioxide snow.

In the majority of these circumstances the influence of cold surpasses the purely physical reaction of the tissues to lowered temperature. Beyond the physical effect the first result of cold is to produce contraction of the blood-vessels. This results in ischemia and local tissue anoxemia. There is less blood in the capillaries and therefore further reduction of the heat brought to the part. If the application of severe cold persists, tissue death occurs. Among the cells affected are the intimal cells of the blood-vessels. Death of these leads to intracapillary thrombosis, which still further adds to the local ischemia. These combined influences may then eventuate in more generalized necrosis and gangrene. Aschoff produced experimental mummification in a rabbit's ear by exposure to a temperature of 16° to 20° C. for periods of five and ten minutes.

When the length of exposure or degree of cold has not been sufficient enough to produce irreversible necrosis, further pathologic processes may ensue after removal of the cold. As the tissues warm up, or thaw out, if they have been frozen, there is a reactionary dilatation of the capillaries with resultant hyperemia. But because of the great disturbance in the fluid and electrolyte balance and the increased capillary permeability there is further swelling with fluid accumulation and increase of leukocytes. This gives the typical picture of acute inflammation. Congestion causes the part to become livid and purplish. The disturbed nutrition and anoxemia are reflected in the damaged tissue by chapping of the skin surface, peeling, and the formation of blisters. The clinical picture of this reaction stage is called pernio or chilblain. A part once so damaged shows a tendency to recur more readily on subsequent exposure.

The observation that certain people react more severely to cold than others and that some show lesions of an angioneurotic nature has led to the belief that there is such a phenomenon as sensitization to cold. There is at present no indication that this sensitization is a true sensitization in the strict use of the term.

In these individuals the exposure of a local part of the body to cold, such as dipping the hands in cold water causes local swelling or urticarial wheals in the skin of the part or some other area of the body. These reactions do not appear until the source of the cold has been removed. There are moreover certain cases in which general symptoms occur following local exposure.

Levine[1] classifies the reactions into three types:

1. Those showing only local symptoms as above.

[1] Levine, H. D.: Arch. Int. Med., 56, 498, 1935.

2. Those with local and general systemic reactions with fall in blood-pressure, rise in pulse-rate, flushing of face and ears and a tendency to syncope. There may also be headache, rigor, dyspnea, cough, generalized aching pains, transient blindness and hemoglobinemia.

3. Those showing systemic reaction without local lesions at the point of exposure. Such individuals may have asthmatic attacks, vasomotor rhinitis, photophobia, abdominal pains, and scattered areas of pruritis, urticaria, angioneurotic edema and eczema. Shock may supervene.

Although a number of theories have been advanced to explain both local and general sensitization reactions they all tend to assume that there is some as yet unidentified chemical agent produced from the tissue cells by the physico-chemical changes brought about by cold.

Supporters of the immunologic theory base their belief on experimental evidence showing that antigens can be passively transferred from sensitive to non-sensitive subjects and the development in the latter of cutaneous wheals on the application of cold. They apply the same theory to the development of paroxysmal hemoglobinemia. The immunologic theory postulates the presence of hemolytic and dermolytic amboceptors and the formation of hemolysin and dermolysin. These combine with the membranes of cells, alter their permeability, and release cell contents into the intercellular medium. Hemolysins acting in this way on erythrocytes can therefore produce hemoglobinemia and dermolysins permit the formation and accumulation of edema fluids.

Vaughn and others explain the local reaction as due to local axone reflexes which result in the formation of wheals and dilatation of capillaries. The systemic reaction they believe to be due to a histamin-like substance, produced by cold in the local tissue, and carried throughout the body by the circulation. The latter explanation is supported by the fact that a tourniquet placed above the part before it is exposed to cold prevents the development of general symptoms in sensitive subjects.

Duke observed that sensitivity to cold is lost in the presence of fever and therefore considers the sensitization reaction a disturbance of the general heat regulating mechanism.

The formation of a vasodilator substance in the local tissues has a strong proponent in Horton.[1] He has demonstrated that histamin or a histamin-like substance is liberated by cold from tissue cells. This he believes is due to breakdown of certain molecules of the skin, subcutaneous tissues or muscle cells. He, like Vaughan, has shown that a tourniquet will prevent general symptoms. Horton draws the general conclusion that the phenomenon is bound up with

[1] Horton, B. T.: Proc. Staff Meeting Mayo Clin., 9, 447, 1934.

the whole question of "tissue substances" and draws the comparison of the liberation of acetylcholine by stimulation of the vagus, epinephrine by the sympathetics, and Cannon's sympathin E and sympathin I which escape from cells and exert effects in distant organs.

Many investigations have shown the effects of local chilling on distant parts of the body. Winslow and Greenberg,[1] Nedzel,[2] and Mudd, Grant and Goldman,[3] presume that this is brought about by vasomotor reflex. Nedzel, interesting himself largely in the kidney, showed reflex vasoconstriction and vasodilation in response to skin chilling. This was accompanied by increased permeability and permeation of the endothelial cells of the capillary blood-vessels. Winslow showed that a cold draught on the feet caused a decrease in the temperature of the nasal mucous membrane and cold on the back of the neck increased it. Mudd *et al.*, demonstrated reflex vasoconstriction and ischemia of the palatine tonsils, palate and pharynx with lowering of their temperature following chilling of the body surface. There is increasing evidence that such disturbances of circulation in internal organs as shown by Nedzel in the kidney and depression of temperature in the naso-pharynx may act as predisposing causes in bacterial diseases of these organs. It is assumed that the changes favor growth, virulence, or invasibility of the organisms which may be present in or gain access to these regions.

Exposure of the body generally to a cold environment calls upon the entire heat-regulating mechanism for adjustment to it. Under these circumstances body heat must be conserved. Although the surface of the body is actually chilled it is prevented from falling to marked degrees by exercise. The surface capillaries contract so that there is a lessening of blood volume in the skin and an increase in the interior of the body, especially in the muscles. Benedict and Parmenter[4] have shown that exposure to cold in spite of muscular exercise results in a drop in the skin temperature of the extremities but maintains that of the body trunk.

Under circumstances which permit prolonged exposure without exercise metabolism is depressed, the temperature of the body sinks, the skin becomes livid, the muscles stiffen and the pulse is small and weak. If the temperature of the body falls to 20° C. *(68° F.)* or *18° C. (64.4° F.) death* ensues.

Heat.—The limit of tolerance of tissue cells to high temperatures appears to be that at which cell proteins begin to coagulate. The local effects of heat therefore are not serious until this point is reached. When coagulation has occurred there is little probability

[1] Winslow, C. E. A., and Greenberg, L.. Am. Jour. Hyg., 15, 1, 1932.
[2] Nedzel, J · Jour Urol , 31, 785, 1934
[3] Mudd S , Grant, S B , and Goldman, S. J . Jour. Exper. Med., 32, 87, 1920
[4] Benedict, F G , and Parmenter, H. S : Am Jour. Physiol., 87, 633, 1929.

that the colloidal state of the proteins is reversible. The primary effect of the coagulation of proteins within cells is disarrangement of the equilibrium between the soluble and gelled colloids. This influences metabolic processes generally and interferes with the functions of the different parts of the cytoplasm, nucleus and other cellular structures. Osmotic pressures, cell membrane tension and electrolyte exchange are altered with serious consequences.

The coagulation-point of proteins is not much above that which can be well tolerated by the bare hands. It is necessary therefore for such temperatures to be maintained for some time in order that the temperature of the cells may be raised to the same degree as the environment.

In vitro experiments by Aschoff[1] on isolated cells showed that leukocyte activity, as measured by phagocytosis, was maintained *at 40° C. (104° F.), but was lost at 50° C. (122° F.) and that at the* latter point they coagulated and disintegrated. At 50° C. (122° F.) erythrocytes contract and develop an irregular, thinned surface from which extend small pedunculated nodules which may eventually be thrown off into the medium. At 60° C. (140° F.) the erythrocytes become globular and begin to show hemolysis. Hemolysis may begin at lower temperatures if the cells are exposed for a long time. When the temperature reaches 70° C. (158° F.) the red cells no longer extrude nodules but become globular and coagulate.

Werhovsky[2] found that the tissues of living animals were affected by rising body temperatures in the following sequence—blood, liver, kidneys, myocardium. Within the limits of life of the animals the other tissues showed little or no structural injury.

Scalds from highly heated liquids, and *burns from contact with* superheated objects and flames, produce immediate death of cells by instantaneous coagulation, rapid dehydration or actual carbonization. In all, the end-result is necrosis.

It is customary to classify burns, according to the extent of injury into first-, second- and third-degree burns. The tissue destruction is gross, extends beyond the cells, and involves all of the mechanisms of tissue nutrition, repair and regeneration. The reader is referred to standard surgical works for the clinical appearance and outcome of burns.

Of particular interest from the point of view of causation in disease is the occurrence of ulcers in the upper intestinal tract following some burns of the skin surface. These ulcers, described by Curling and bearing his name, occur in the duodenum at some point above the opening of the bile duct. They are small, clean-cut and deep and may go on to perforation.

The most generally accepted explanation of their pathogenesis

[1] Aschoff, L.: Pathologische Anatomie, Jena, 1923.
[2] Werhovsky: Ziegler's Beitr., 18, 72, 1895.

rests on vasomotor spasm. This may originate reflexly, or through the action of histamin or a histamin-like substance released at the site of the burn. The vasomotor spasm occurs in the end arterioles of the duodenum and interferes with nutrition. Moynihan is of the opinion that septic emboli from the burned area lodge in the arterioles of the duodenum and set up infected foci. Due to the dehydration resulting from extensive burns the plasma viscosity is increased and this is believed by some to favor thrombosis in the duodenal and other vessels.

Death from severe burns (which is said to follow when over one-third of the skin surface is involved) is not yet satisfactorily explained. That it may be due entirely to the mechanisms of shock is quite generally accepted, but there are some who believe it results from the absorption of toxic material from the burned skin.

The response of the human organism to hot environmental temperatures is accomplished through its heat regulating mechanism. While the body is exposed to this external heat it continues to produce its own internal heat, thus necessitating a call upon physiologic processes to aid in heat dissipation and elimination. Under natural conditions the problem of response to heat is complicated by the influence of humidity and air movement. Experimental work under controlled conditions have given some valuable information regarding the reaction of the body to heat alone.

Lee[1] has given an excellent summary of the nature of the adaptive reaction to heat, and his work will be followed freely in this discussion.

Lee considers adaptive reaction in three stages:

1. Immediate passive reactions (independent of life)—rise of skin temperature, increased evaporation of surface moisture.
2. Primary active adaptations—cutaneous vasodilation, sweating, primary water shifts.
3. Secondary active adaptations—rise of body temperature, alterations of endocrine balance, increased pulmonary ventilation, decreased appetite.

The first stage is accomplished by the physical factors of radiation, conduction and convection, and applies to the human organism as it does to any physical body. In the second stage neuro-vascular response mechanisms appear to be the major factor concerned. These responses are body wide and are undoubtedly under nerve control. The primary effect appears to be on nerve endings in the skin. Benson[2] is of the opinion that these cutaneous "hot spots" are stimulated by environmental heat and transmit their impulses to other organ centers by reflex action. The discovery of "heat regulating centers" in the medulla makes it probable that they act

[1] Lee, D H K. Trans. Roy. Soc Trop. Med. and Hyg., 29, 7, 1935.
[2] Benson, S Arch. Phys Ther., 15, 303, 1934

as intermediating controls between the skin receptors and the responding tissues and organs. At any rate, the end response is one of cutaneous vasodilation, increased gland activity (especially the sweat glands), and increase of surface blood volume. With these changes there is increased heat loss through the body surface which is efficient enough unless the hot environment is excessive or other factors are present which interfere with the normal mechanisms. When the heat loss cannot so compensate for heat gain the temperature of the body will rise. It is then that Lee's third stage of adaptive reaction comes into play by depressing the metabolic activity of the thyroid and suprarenal medulla. This depression, which Lee cautions has been ascribed without proof to nerve stimulation or direct effect of blood temperature, reduces metabolic activity of the whole body. This tends to compensate for rise of body temperature.

Under normal conditions 75 per cent of the heat loss from the body is from the skin and 25 per cent through pulmonary ventilation. Although the latter is increased with rising body temperature, the loss by vaporization of moisture from the lungs remains relatively insignificant. With the lowered basal metabolic-rate there is less need for high-caloric intake. By some unexplained mechanism this is reflected in the psychic response for caloric demand *by diminished appetite.*

Four important system functions are involved in the mechanism of heat control: (1) Water metabolism, (2) circulatory system, (3) electrolyte balance, and (4) acid base equilibrium.

Water metabolism is disturbed by increased water loss through *sweat gland activity. Unless this is resupplied, dehydration will* result. Vasodilation increases the capacity of the circulatory system. If dehydration prevents the maintenance of the normal ratio of blood volume to system capacity, circulation will be impaired and the blood-pressure will fall.

Chloride is concentrated in the body by the loss of large amounts of hypotonic sweat. If now the fluid loss is replaced by water the chloride in the body fluids will be diluted to a lower concentration. The body reserve of chloride is then called upon to raise the concentration which may eventually result in exhaustion of body chloride by continued sweating. When there is such exhaustion and water is taken in large quantities the concentration of chloride will be seriously lowered and produce a clinical picture of water intoxication.

All of the above changes and the adaptations to them are on the physiologic level, that is, they are reversible under the normal mechanisms ordinarily concerned in the functions involved.

Lee describes subsequent changes, which surpass the physiologic limits, as the breakdown between the body and its environment

(temperature environment). He ascribes the breakdown to four critical events: (1) Hyperpyrexia, (2) circulatory insufficiency, (3) electrolyte imbalance, (4) super-dehydration.

Hyperpyrexia is reached, Lee says, when the mean temperature of the body is such that the continued life of some vital tissue is endangered thereby. This point, as previously stated, appears to be the temperature at which proteins begin to coagulate (108° F.; 42.2° C.). Neuroglobulin has a coagulation-point at this temperature so that the nervous system is one of the first to suffer.

Predisposing causes of hyperpyrexia will be anything that interferes with heat loss or augments heat production. With a body temperature approaching 108° F., bright sunshine on the head and neck may raise the temperature locally above the critical point. Infection, alcoholism, hyperthyroidism, certain drugs, and severe physical work act, according to Lee, in this way. He cites heavy clothing, inhibition of sweating, and dehydration as interfering with heat loss.

Circulatory insufficiency (Lee) is the failure to maintain the blood supply necessary for the continuance, without marked impairment, of the bodily activities going on at the time. This becomes manifest when the depleted fluid volume of the blood has embarrassed the circulatory mechanism to the point where it cannot meet additional demands such as heavy meals, alcoholism, heavy exercise, long-continued standing, dehydration and emotional disturbances.

Electrolyte imbalance becomes serious when the serum chloride concentration falls to 365 mg. per 100 cc. or less.

Lee defines super-dehydration as the loss of water from the body to such an extent that continued existence is threatened, should replacement not be effected. The critical level probably lies at about 20 to 25 per cent of body weight. Such water loss impairs circulation and leads in turn to disordered metabolism, acidemia, disordered nervous function and diminished heat loss.

The combination of these disordered functions results in coma and death.

In concluding his discussion, Lee parallels the four modes of breakdown and their clinical terminology with the four chief physiologic system crises which have been described.

Crises	*Modes of Breakdown*	*Clinical Synonym.*
1. Hyperpyrexia	Hyperpyrexia	True heat stroke
2. Circulatory insufficiency	Heat exhaustion	Heat prostration
3. Electrolyte imbalance	Heat cramps	Miner's cramp; Stoker's cramp
4. Super-dehydration	Dehydration	

CHAPTER XXXI.

THE DEFENSE AGAINST COLD AND HEAT.

With the exception of heated environmental air, the prevention of local freezing, body chilling, local burns and scalds is synonymous with protection. Since local freezing occurs under natural conditions it should be a simple matter to reduce the opportunities for it by protective coverings such as mitts, gloves and ear pads. Tight shoes, restricting garters, and too heavy stockings compress the feet, diminish the circulation and impede the return of venous blood. They should be avoided when exposure to cold for long periods is anticipated. This is especially true in the presence of pre-existing circulatory disturbances in the extremities and for those who have a hypersensitivity to cold or have previously suffered from chilblains.

Workers in ice plants and refrigeration rooms require similar protection.

Chilling of the body should be prevented by adequate heat-retaining clothing. Wool and silk are better than cottons. For those who can adapt themselves well to low temperatures there can be little harm in wearing clothing as light as may be compatible with comfort. Lividity of the skin of any part should be a warning that chilling has occurred.

Cold draughts in general should be avoided because of the reflex disturbances in other parts. There is much to indicate that localized cooling from this cause has some bearing on liability to infections, particularly those of the respiratory system.

Children should be warned of the danger in the stunt of touching their tongues to cold metals such as railroad tracks, auto-rims, etc., and the sucking of dry ice. The avoidance of danger from heated articles, boiling liquids, and fire resolves itself into the same factors as the prevention of accidents in general. Specifically, it is knowledge and anticipation of known hazards. It involves also the use of safety devices and safety measures wherever heat is employed as in the use of flat-irons, heaters and burners, electric arcs, open flame illuminators, matches and lighters. Whenever it becomes necessary to come into contact with high heat, as in many industries and occupations, it is necessary to resort to protective clothing of thick material or asbestos or the use of insulated handles, tongs and other instruments by which objects can be handled indirectly.

Successful adaptation to residence in hot environments can be enhanced by intelligent consideration of the physiologic adjustments

necessary for normal heat control. This implies the use of light clothing, adequate protection of the head against the direct rays of the sun, covering of the abdomen to prevent local chilling, avoidance of sitting inactive in damp clothing, wholesome nourishing food without excessive caloric intake, moderation in alcoholic drinks, the use of cool or warmed drinks in amounts equivalent at least to fluid loss, and care of the bowels and other eliminative organs. To all of these can be added attempts to improve the environment by proper attention to ventilation in buildings and the use of artificial methods of cooling and creating air movement. In the use of the latter, care should be taken to avoid too direct chilling by cold draughts.

When workmen are required to work in very hot, dry atmospheres it is necessary to keep up their fluid loss by the ingestion of water at frequent intervals. In order to prevent hypotonicity they should take sodium or potassium chloride at the same time. They should not work without clothing unless the atmosphere is damp. Light loose clothing retains sufficient moisture to aid evaporation, which in turn has a cooling effect. Under no circumstances should they be allowed to consume copious draughts of water on coming out of the heat. The sudden intake of large volumes of liquids still further embarrasses the adjusting mechanisms. The kidney activity has been reduced under the heat and is not able immediately to take on such increased demand. Failure to comply with this precaution may bring on symptoms of water intoxication.

CHAPTER XXXII.

THE EFFECT OF WATER-VAPOR IN AIR (HUMIDITY).

HUMIDITY is the amount of water-vapor in air. Although the common conception of humidity is moisture or dampness of the atmosphere, this is erroneous, because water-vapor is a gas. Moisture appears when the gas condenses. Haze, mist and fog are optical effects of minute droplets in suspension in the air. Rain, hail, snow and dew are visible condensations of water-vapor.

Humidity can be measured in absolute terms of the amount of water-vapor in a unit volume of air. English hygrometric tables give this in grains of water-vapor per cubic foot of air. This measure is the *absolute humidity* of air.

Because the amount of water-vapor in air varies with the temperature and pressure of the latter, humidity can be expressed in terms of this relationship. Air at a given temperature and pressure can contain only a certain amount of water-vapor before the latter begins to condense. The point at which condensation occurs is called the saturation-point. If the air at this temperature and pressure is considered as containing 100 per cent of its possible content of water-vapor, then anything less than this amount of water-vapor in the same air at the same temperature and pressure can be expressed as a percentage of its possible saturation. This *percentage is the relative humidity. This measure always refers,* therefore, to a given air temperature and air pressure. It is simply the percentage expression of the amount of water-vapor present to what could be present if the air were saturated. A relative humidity of 85 means that the air at the given temperature and *pressure is 85 per cent saturated. It can still take up 15 per cent* more moisture by evaporation from some source. This smaller percentage represents then the evaporating power of the air. If the relative humidity is 98, then it can still take up only 2 per cent more moisture and will be relatively ineffective as an evaporating *medium.*

If now the vapor content is kept constant and the temperature is gradually lowered, the per cent saturation becomes greater and greater until it again reaches the point of complete saturation. At a fraction of a degree below this point condensation takes place. *The temperature at which this occurs for a given humidity is called* the *dew-point.*

Evaporation of moisture produces cooling. Since the amount of evaporation possible by a given sample of air depends on the amount

of moisture it can still take up it is possible to allow it to evaporate as much as it can and measure the amount of cooling which this produced. This is the principle of the psychrometer. This apparatus consists of two thermometers held side by side in a frame which can be twirled around rapidly in the air. One thermometer measures the constant temperature of the atmosphere. On the bulb of the other theromometer is slipped a muslin jacket which has been soaked in pure water. The two thermometers are termed, respectively, the dry and wet bulb thermometers.

When the apparatus is swung around in the air the air takes up all of the moisture it can from the muslin jacket of the wet bulb. This evaporation extracts heat and cools the wet-bulb thermometer while the dry bulb remains at the temperature of the air. In practice the psychrometer is twirled for twenty to thirty seconds, then the temperatures are rapidly read and the apparatus is twirled again and reread at intervals until two subsequent readings reveal no further depression of the wet-bulb thermometer. The difference between the dry and wet bulb readings will measure the cooling effect at this temperature brought about by the evaporation of as much more moisture as the air is capable of holding. This difference can be converted into *relative humidity* by calculation, or, more readily, by reference to tables prepared for the purpose. In refined determinations the psychrometer must be protected during twirling from solar and body radiations, and the readings must be corrected for atmospheric pressure.

Approximate readings of the dew-point can be obtained from the dry- and wet-bulb temperatures. The dew-point is as many degrees below the wet bulb reading as the wet bulb is below the dry bulb. If dry bulb reads 90 and wet bulb 85, the dew-point is 80. That is, if the air temperature falls to 80 condensation will take place.

It must be understood that the amount of water-vapor in air is not an inherent physical property of air. Air may be completely "dry," that is, it may have an absolute humidity of zero. On the other hand, water-vapor may fill a space entirely devoid of air.

The amount of water-vapor in air is an end-result of the operation of other factors which initiate the evaporation of water from some source, facilitate its transportation to and from a given locality, and determine the capacity of the air to "hold" water-vapor. These factors will be those which influence temperature, wind, sunshine, available water, vegetation, etc., and to some extent altitude and barometric pressure.

Humidity may be raised or lowered by artificial means. The atmosphere in rooms may have its water-vapor content increased by passing the influx over a moist surface or through actual water sprays or by changing the temperature to raise the saturation-point.

The temperature of the walls is of great importance, for they act as condensation surfaces on which moisture is deposited. If the *temperature of the walls is raised, they give up this moisture again* to the atmosphere, and so act in part as an automatic humidity control. Rosenau notes that the walls may contain as much moisture as all the air in the room.

The science of ventilation, now largely turning toward the practice of "air-conditioning" has reached the point where air of any temperature and humidity may be obtained artificially. Its principles depend on the control of those factors known to affect saturation and include, therefore, artificial heating or cooling, addition or removal of moisture, and controlled air movement and circulation.

The physiologic effect of water-vapor in the atmosphere becomes of importance to the individual under his ordinary conditions of life and when subjected to extraordinary degrees of saturation under artificial working and living conditions. It influences him in his home, in the factory, the workshop, the office, the theatre, and out-of-doors in climates with extremes of humidity, as in the moist *tropics and arid deserts.*

Seldom, except under experimental conditions, can the humidity factor be separated from the factors of temperature and air movement. The functional relationship of these three is so intimate that they will be dealt with collectively later under the effects of climate and weather (page 349).

As to humidity, *per se*, the point of greatest physiologic significance is not the amount of water-vapor in the air but the amount of water-vapor which the air can contain under given conditions. For this reason relative humidity is of greater practical importance than absolute humidity; it expresses the potential amount of water-vapor which can still be taken up. Physiologically, this is bound up with evaporation of moisture from body surfaces (lungs and skin) and the mechanism of heat control.

Fundamentally, still air at a constant temperature will permit evaporation of perspiraton and expired water-vapor proportionately to the percentage saturation of the atmosphere. Since evaporation has a cooling effect on the surface of the body from which the heat is extracted the amount and rate of evaporation from the skin will determine the cooling effect on the skin. If the per cent saturation of the atmosphere is low, evaporation and, therefore, cooling will be more effective than in an atmosphere of high relative humidity. The heat loss in still-air is accomplished by radiation and conduction (convection implies air currents). The extent to which these are effective determines to a great degree the demand put upon the heat mechanism of the body.

In the human the rate of evaporation and the efficacy of radiation and conduction are markedly affected by clothing.

Clothing acts as a heat-absorbing and eliminating body and also takes up moisture. Since the body is active in the production of heat and elimination of moisture, clothing acts by enhancing or preventing the absorption of heat and moisture from the layer of air between it and the body. Its efficiency in controlling the physical state of this air jacket about the body will depend on the activity of the body, the temperature and humidity of the outside atmosphere, and the physical qualities of the clothing itself. When the relative humidity of the air is low and the temperature is low, heat-retaining clothing is necessary. With low temperature and high humidity most comfort is obtained by clothing which absorbs moisture but retains heat. At high temperature with low humidity clothing which is light and a poor absorber of heat is most desirable, while if both temperature and humidity are high the clothing should be moisture-absorbing in addition.

The effect of baring part of the body in hot humid weather is to facilitate direct evaporation and cooling of the exposed part, and reflex cooling of covered parts by reduction of their blood supply and lowering the activity of the sweat glands.

CHAPTER XXXIII.

THE MECHANISM AND EFFECT OF AIR MOVEMENT.

AIR in motion over the surface of the body occurs as a result of: (1) winds produced by the meteorologic factors of the environment (climate and weather); (2) local air currents (draughts) set up by differences in temperature and air pressure in the immediate atmosphere (*windows, ventilators, heating units, etc.*); (3) *forced air* currents produced by artificial blowers and suction apparatus (fans, etc.); (4) relative motion of air created by movement of the body through it (speed through the air).

Irrespective of the origin of the moving air, it is in effect, the mechanical replacement of air molecules in contact with and surrounding the body by new molecules. Since the human body is constantly producing and eliminating heat, temperature gradients develop between it and the molecules of air surrounding it. As the air takes up heat and absorbs moisture from the body it becomes warm and moist, approaches the temperature of the body surface and develops a high relative humidity. If the air is still it soon acts as a jacket which prevents further loss of heat and evaporation of moisture from the body. When the air is in motion new molecules of air replace the old and establish new temperature gradients. It is the repeated satisfaction of the new gradients in the disturbed equilibria between the body and moving air which removes heat by convection and produces cooling by evaporation.

Moving air crossing the surface of the body therefore favors heat loss and evaporation of moisture. As a result, it involves the heat controlling mechanisms of the body generally or influences local body heat.

The important influence of climatic winds depends on the physical state of the moving air. The trade winds, siroccos, mistrals, foehn, monsoons, chinook, khamsin and leveche, are more or less seasonal mass air movements over different parts of the globe and are either hot, cold, moist or dry. Because of these physical properties which are sometimes extreme, the areas affected are subject to the periodic influx of prevailing winds which favor evaporation and temperature loss of bodies subjected to them or surround the bodies with air which is already hot and humid.

Their effects are general and will be dealt with more particularly in the discussion of the climate complex (page 349).

Local draughts caused by open windows, fans, etc., are repeatedly referred to as the cause of stiff neck, lumbago, neuralgia, myositis,

PRINCIPAL SEASONAL WINDS OF THE WORLD

Wind	Place	Blowing from	Season	Causes and Characteristics.
Monsoon	Asia, Australia, West and So. Africa	Southwest Northeast	Hot season Cold season	Corresponds to diurnal winds due to heating and cooling of land and sea areas. Moist, sea-wind. Same seasonal cause. Dry, land-wind.
Foehn	Valleys of Alps, northern slopes	South	Winter most frequently	Heavy, cold, dry winds blowing off the Alps and heating up by compression in the lowlands, giving a hot, dry wind erroneously believed to come from the Sahara.
Chinook	West slopes of Rocky Mountains	Southwest	Winter most frequently Summer	Dry, warm (due to cyclone passing northward in Pacific Ocean) Dry, cool.
Mistral	French Mediterranean; Rhone Valley, Gulf of Lyons	Northwest	Winter	Due to high pressure over French plateau or cyclonic low in the gulf. Cold, dry, piercingly intense, brilliant sunshine.
Bora	Adriatic Sea, Dalmatian coast	North, northeast	Winter	Due to passage of cyclonic low in Mediterranean, drawing cold wind down from the mountains. Cold and violent.
Sirocco I (False Sirocco)	Mediterranean region	North	Winter	Associated with Mediterranean cyclones, moist, cloudy and rainy.
Sirocco II	Sicily, So. Italy	South, southwest	Winter	Dry, dust-laden from No. African deserts.
Simoon	Algeria, Syria, Arabia	South; southwest	Winter	Dry, dust-laden from No. African deserts
Khamsim	Egypt	South, southwest	March, April, May	Dry, dust-laden from No. African deserts.
Leveche	Spain	Southeast, south	Winter	Dry, dust-laden from No. African deserts.
Leste	Madeira	Southwest, east	Autumn, Winter and Spring	Dry, dust-laden from No. African deserts. Lowers relative humidity at Funchal to 20.
Tropical cyclones (Hurricanes)	Caribbean area, Indian Ocean, China Seas and So. Pacific	Travel S E. to N.W. and then tend to turn toward N E	Aug., Sept., Oct.	Circular storms arising in the Doldrums in Western Hemisphere and tropical seas in Eastern Hemisphere.
Northers	North America	North; northwest	Autumn, Winter	Anticyclones of hurricane force.

fibrositis and many other afflictions grouped under the meaningless term, rheumatism. The exact part which cooling draughts play in the causation of these conditions has not been determined, but it *is assumed that they act as trigger mechanisms. By this is meant* the presence of some underlying metabolic, nutritional, or infected state involving the fibrous septa and sheathes of muscles, nerves, tendons, joints, and vascular connective tissues, which is aggravated by the local effects of cold, or cooling, moving air. Although the etiology of these "rheumatic" manifestations is not known, it appears that local tissue chilling can alter the colloid and chemical equilibria by *acting directly at the point of chilling, or reflexly on remote parts.* Grave doubts exist that cold draughts can cause any such changes in tissues other than those already the seat of metabolic or inflammatory pathology.

In a general discussion on fibrosis held at a meeting of the Royal Society of Medicine (London) in 1925, it was suggested that rheumatic symptoms of the type under consideration were probably due *to tissue sensitization from low-grade foci of infection and that the* manifestations commonly appeared following exposure to cold. Recent text-books of medicine carry on the belief in this assumption.

Strong winds with a velocity of over 25 miles per hour "cut off the breath" when they blow directly in the face of the subject. Physiologically this means that the moving column of air enters the respiratory passage with a pressure in opposition to the normal expiratory pressure. (A 50-mile wind raises the atmospheric pressure 0.1 inch; a 100-mile wind 0.4 inch.) As a result, accessory muscles of expiration must be brought into play. Under wind forces of much greater velocities as experienced in hurricanes, typhoons, and rapid modes of travel the embarrassment to respiration may be so severe as to cause marked carbon dioxide loss or even acapnia. Bauer[1], in criticizing the conclusions of Geigel[2] that airplane pilots would be just able to maintain respiratory balance against exposure to a wind speed of 80 meters per second (173 m. p. h.) questions the assumption that a powerful wind could entirely prevent respiration. He bases his doubt on the fact that the wind force would help collapse the chest and that the chest would be subject to the same pressure internally and externally.

Aggazzotti and Gabotti[3] found that strong winds caused both slowing up and acceleration of the pulse with unevenness in rhythm, modification of the pulse wave, and reinforcement of the cardiac pulsation. These investigators believe such changes are all reflex in nature.

[1] Bauer, L. H.: *Aviation Medicine*, Baltimore, Williams & Wilkins Company, 1926.
[2] Geigel: Münch med. Wchnschr., 34, 1253, 1917.
[3] Aggazzotti, A., and Gabotti: Gior. di med Mil., 67, 107, 1919.

At speeds over 100 miles per hour, airplane pilots and automobile racers must protect themselves from the high air force which their travel creates. If they do not use helmets or goggles the soft parts of the face are ballooned out to a painful degree. The eyelids are blown wide open and overstretched and the cheeks inflated with the lips widely parted so that it is impossible to close them. The backward pull on the hair creates a tingling of the scalp which, if long continued, results in numbness.

Bauer states that at 250 miles per hour, if a pilot should hold his arm out it would be broken and, should he stand up with his head above the cockpit, he would be knocked over and his neck probably broken.

In the presence of antecedent disease of the cardiovascular system exposure to heavy winds, especially cold winds, and the necessity to stand up or try to move against them, is liable to precipitate acute cardiac decompensation, vascular hemorrhage or even sudden death. It is one of the common terminal events of patients with angina pectoris in northern climates.

CHAPTER XXXIV.

THE INFLUENCE OF CLIMATE AND WEATHER.

CLIMATE and weather are manifestations of the total state of the meteorologic and atmospheric conditions of a given area, the first representing the average quantitative measurements of the meteorologic factors over a long period of time (generally years, decades, or centuries) and the second during short periods of days, weeks or months. If the climate is represented graphically as a long, more or less undulating curve, weather would be the closely spaced intermediate points above and below the curve and from which the curve was plotted. In common terms climate implies a fairly uniform picture of the year by year distribution of seasonal heat and cold and average humidity, sunshine, rainfall, and windiness; weather connotes periodic storms, winds, clear and cloudy days, hot, cold and humid days and changes in barometric pressure.

The individual is more immediately and consciously concerned with weather than with climate because it limits and directs his daily activities to a greater extent. Climate, on the other hand, is of greatest importance to the race for the length of the climate curve permits physical, social and cultural adaptations in the race, which are not possible in the span of a single life.

Both climate and weather are complexes of the same meteorologic factors; temperature, sunshine, humidity, precipitation, ionization of the atmosphere, air movement and barometric pressure. Non-climatic elements which determine climate and weather are latitude, altitude, land and water masses, vegetation, mass air motion, mountains, volcanic action, sun altitude and zenith distance, the sun's distance from the earth, sun spots and possibly other unknown factors, such as those which determine the advance and recession of the polar ice caps. It is becoming more certain that man's own efforts can change the meteorologic conditions of limited areas by draining land or flooding it and by denuding it of protective vegetation.

Although much that is written on the influence of climate on civilization cannot be accepted there is nevertheless a close correlation which is suggestive of some influence of climate on human activity. It seems very probable that in general the temperate climates are more conducive to heightened physical effort than the heat of the tropics and that there are actual enervating effects from certain combinations of heat and moisture. On the other hand, human ingenuity and intellectual capacity do not seem to have

suffered in the past from prolonged living under what seem to be most undesirable climatic conditions. It may be granted, however, that climate may put obstacles in the way of progress and in some instances may have actually aided progress and civilization.

The part played by climate in conditioning human behavior is highly pertinent to man's social and cultural development. The present concern, however, is with the influence of the combined meteorologic factors of man's environment on his physiologic mechanisms. With the exception of ionization of the atmosphere, each of the factors has been dealt with individually in the preceding pages of this section. No one meteorologic factor operates entirely independently of the others on the human economy. Three of them are so interwoven in their effects as to constitute the most important environmental triad to which the body is exposed. They are, temperature, humidity and air movement. The reason they are collectively so important is because they each primarily affect the heat regulatory mechanism, and this is the most important mechanism by which the body adapts itself to changing intensities in its atmospheric environment.

Reasoning from analogy it has been assumed that the human, like other organisms, has a biologic optimum in its range of external temperature and humidity. Huntington[1] has attempted to approach the problem for man by measuring physical and mental output under different combinations of temperature and humidity. In 1932 the American Society of Ventilating Engineers[2] studied the question by measuring metabolic activity, pulse-rate, rectal temperature, change in body weight, blood-pressure, and work output under variable temperatures and humidity.

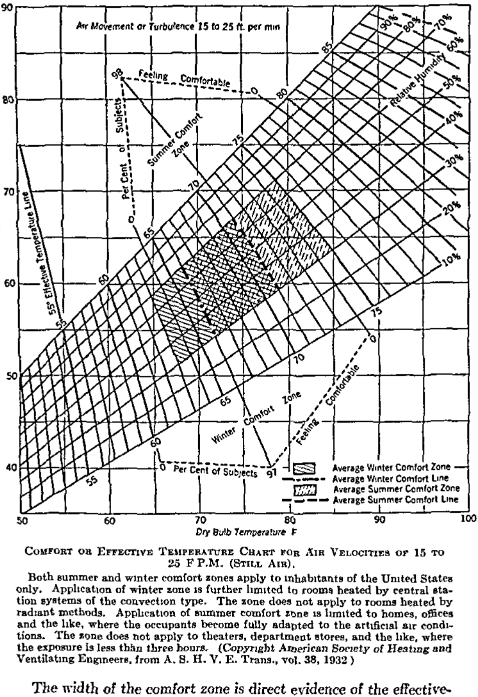
Huntington's optimum conditions are a temperature ranging from 65° to 70° F. with a relative humidity of about 60 per cent. The "effective temperature" range arrived at by the Society of Ventilating Engineers is 63° to 71° F. in wintertime and 66° to 75° F. in summertime with a relative humidity of 30 to 73 per cent. The air velocity at these effective temperatures varies from 15 to 25 feet per minute.

Within these limits the same degree of comfort is obtained by lowering the relative humidity as the temperature is raised or *vice versa*. A chart prepared by the Society of Ventilating Engineers shows the combinations at wet and dry bulb temperatures, and relative humidities at which most people feel at comfort. The areas blocked out by the limits of these coördinates are called the comfort zones. Beyond these limits discomfort is felt whether the temperature and relative humidity are both above the upper or below the

[1] Huntington, Ellsworth Civilization and Climate, New Haven, Yale University Press, 1915

[2] Trans Am Soc Ventilating Eng, p. 38, 1932.

lower limits or whether they are widely separated with one above and the other below the comfort zone.



Comfort or Effective Temperature Chart for Air Velocities of 15 to 25 F.P.M. (Still Air).

Both summer and winter comfort zones apply to inhabitants of the United States only. Application of winter zone is further limited to rooms heated by central station systems of the convection type. The zone does not apply to rooms heated by radiant methods. Application of summer comfort zone is limited to homes, offices and the like, where the occupants become fully adapted to the artificial air conditions. The zone does not apply to theaters, department stores, and the like, where the exposure is less than three hours. (*Copyright American Society of Heating and Ventilating Engineers, from A. S. H. V. E. Trans., vol. 38, 1932*)

The width of the comfort zone is direct evidence of the effectiveness of the heat regulating mechanism insofar as subjective sensations of comfort are concerned, but gives no indication of the

biologic adaptability of the organism at the extremes of high and low temperatures at varying percentages of humidity. The implication is that the comfort zone represents the region of optimum physiologic activity and output in work and mental effort, and conversely that under conditions beyond the effective temperature limits, physiologic activities are carried on under added strain.

Of no less importance, physiologically, than the effective temperature range, is the variability of the climatic factors. Although the limits of the comfort zone may represent the optimum temperature and water vapor environment it is probable that a monotonous restriction of these factors within such narrow limits is not best for the active working organism.

The importance of changes in the intensity of the individual meteorologic factors has been shown in the earlier part of this section. In each instance it was seen that the greatest physiologic effect was produced by fluctuations above and below the average intensity and that in most instances the extremes approached or surpassed physiologic tolerance. Temperature, humidity and wind had their greatest effects on the heat regulating mechanism; barometric pressure influenced respiratory exchange and cardiac output; extreme cold and heat affected peripheral circulation; sunlight exerted its greatest influence on skin metabolism and secondary general metabolic processes.

In a changing, variable climatic environment all of these factors are concerned and almost every mechanism of the body is disturbed by their shifting intensities. If the changes are not extreme in force or duration and do not surpass tolerance to them, they are in all probability very valuable physiologic stimuli to improved circulation, aëration, digestion, nutrition and oxidation of the tissues, eliminative activity, general metabolic efficiency and therefore a better output of physical and mental work. No claim is made that the truth of this statement is confirmed in detail but many studies confirm the probability of the generalization.

Huntington, Mills,[1] Peterson[2] and others have transposed the experimental studies on the climatic factors to actual climatic conditions throughout the world, past and present, and correlated different climate complexes with such things as the progress of civilization, levels of culture, work output and mental efficiency, the subjective sense of well-being, onset of menstruation and duration of fertility, the incidence of special diseases and diseased states, and other even less measurable aspects of human behavior. A satisfactory review of their findings is beyond the scope of this presentation and the reader is referred to the original sources. A few of the correlations are so significant as to necessitate brief mention.

[1] Mills, C. A.: Living With the Weather, Cincinnati, Caxton Press, 1934.

[2] Peterson, W. F.: The Patient and the Weather, Ann Arbor, Edwards Bros., vols. 1 to 2, 1934.

Mills, with painstaking care, has worked out a coefficient of variability of climate which he has applied to a map of the United States in the same way in which isothermal lines are drawn on ordinary weather maps. By this means he has brought out in relief the areas of greatest diurnal and seasonal maxima and minima, that is, the areas of greatest climatic turbulence, and the opposite state of areas with relatively monotonous climates. On these areas he has superimposed disease incidence and death rates of a number of infectious and non-infectious diseases. Corrected rates for age, sex and racial groups have revealed high figures for arteriosclerosis, hypertension, pernicious anemia, diabetes, nephritis and suicide in the areas of greatest storminess in the Middle and Western Great Lakes Basin. The rates for these conditions in these areas are out of proportion to the general death rates of similar population groups in areas of less storminess. The inference is that the extreme variability of the climate exceeds the needs of the organism and drives some one or more of the physiologic mechanisms beyond their power of adaptation. This is readily conceivable and worthy of continued study. Exception must be made, however to Mills' use of the term "Exhaustive Diseases" as applied to those listed above. It is neither generally believed nor proven that the ordinary conception of exhaustion can be applied to the mechanisms underlying the etiology of pernicious anemia or diabetes. The others on the list come nearer to the idea. Nevertheless, the high correlation with factors which are so able to disturb physiologic activity make it appear reasonable to suppose that excesses of climate can and do play a part in the causation of many diseases.

It may be granted that climate makes a profound difference in the intensity and manifestations of many diseases and may possibly itself initiate certain disease states. This is evidenced in the distribution and clinical types of such diseases as epidemic poliomyelitis, scarlet fever, pneumonia, smallpox, rheumatic fever and tuberculosis. But in these, climatic factors are not necessarily of primary importance.

It is assumed that climate has an important bearing on the incidence and severity of "degenerative" and nervous diseases. Although psychic and social factors cannot be ruled out in the marked improvement of psychoneurotics who have been removed to new environments, there is a strong feeling among physicians that the change of climate is of importance. It is this feeling which is so strongly urged by Peterson in his discussion of the reactive types to meteorologic factors. He calls the human a "Cosmic resonator." By this he means that the receptor mechanisms of the body respond to the rhythm which is evidenced by intervals of alternating vasoconstriction and vaso-dilation. These vascular changes produce phases of anoxemia and widespread alterations of metabolism in all

body functions. Peterson would raise climatic environment to the position of the great determiner of health and activity, and a potent factor in disease. He does not deny the importance of food, infection and other environmental factors.

Whatever may be said in explanation of the effects of climate and weather as a cause of disease there can be little denial of the fact that the health of all organisms is affected by it. The experience of the race confirms the debilitating effect of torrid climates and the exhilaration of cool, dry air. Nor can it be denied that depression comes with a falling barometer, the onset of storms, the long hot summer, or the periodic enervation of the seasonal hot winds.

Gloomy days are depressing, bright crisp days are stimulating; a mild winter brings joy and efficiency and a frigid stormy winter is exhausting. Although much of this may be psychic, anything which is able to affect psychic reactions so profoundly is surely as much of human concern as any of the physical factors which can be analyzed and measured.

Human discomfort brought about through unfavorable climate and weather has caused man through the ages to resort to artificial means of relief. Only recently has the science of ventilation reached any degree of efficiency in preventing uncomfortable indoor temperatures. Air conditioning is artificial weather. It is not yet entirely successful because it is not in general use, and exposure of the body to the effective temperature is not long enough at any one time to permit adaptation to it. Nor has the problem of air motion been entirely solved. In spite of its present inefficiencies, air conditioning is to be championed as a successful approach to a hitherto poorly handled human problem. With it release from many of the undesirable effects of unfavorable climate and weather may eventually be obtained, and conceivably, knowledge may be advanced toward the prevention of diseases in which meteorologic factors play an important part.

CHAPTER XXXV.

THE EFFECTS OF RADIANT ENERGY.

The Nature and Source of Radiant Energy.—When an electron shifts its position in relation to the nucleus of an atom or becomes lost to or taken up by an atom, the shift results in a change in the energies of the atom. Since these shifts are known to be intermittent and discontinuous, it follows that the energy changes must be intermittent.

The quantum theory of radiation states that these intermittent transformations of energy result in the liberation and emission of bundles or quanta of energy which can be propagated through space with the speed of light. The frequency with which they are discharged from the atom determines the interval between them and their wave-length, and their size becomes a function of their energy. The bundles, or quanta, are called photons and possess the characteristics in common with light of obeying the laws of reflection, refraction, polarization and interference, and traveling at a speed of 2.998 by 10^{10} cm. per second (186,000 miles per second).

When rays of visible light pass through suitable media, those of different wave-lengths become arranged in an orderly series of color bands, each band representing light waves of specific wave-lengths. By refined physical experiments it was found that there were other non-luminous rays extending from both ends of the light spectrum, some with wave-lengths longer than those of visible light and others shorter. When it was realized that all of these waves or rays were similar in character and different only in frequency and energy, it became possible to arrange them in a regular series of frequencies now termed the Electromagnetic Spectrum. (All of these waves are spoken of collectively as electromagnetic waves, and their energies as radiant energy.)

The intervals between the emission of quanta energies, *i. e.*, their wave-lengths, are measured in terms of microns and meters.

Roughly, the regions of the electromagnetic spectrum as represented by their common names, correspond to their respective wave-lengths as follows:

Radio communicating waves	20,000 m. (20 km.) to 10 m.	
Broadcasting waves	500 m. to 200 m.	
Short radio waves	200 m. to 10 m.	
Hertzian waves	10 m. to 0.02 cm.	
Infra-red rays (heat rays)	5000 mμ to 800 mμ	
Visible light rays	770 mμ to 400 mμ	Solar radiation, 3000 mμ to 300 mμ
Ultra-violet light rays	700 mμ to 50 mμ	
X-rays	50 mμ to 0.01 mμ	
Gamma rays	0.01 mμ and less ?	
Cosmic rays		

Under natural conditions (using the term natural as opposed to that artificially produced by man) the greater amount of radiant energy comes from solar radiation, which is said to extend from wave-lengths of 3000 mμ in the infra-red, through the entire visible spectrum to approximately 300 mμ in the ultra-violet region. Infra-red rays arise from the radiant energies liberated from heated bodies. Natural ultra-violet rays originate from the sun, solid bodies heated to incandescence, incandescent gases, and electronic disturbances in electric sparks and arcs. Long wave-lengths of Hertzian and radio frequencies may appear under natural conditions when static electricity undergoes motion in electrostatic discharges. *X*-ray frequencies may originate somewhere in the atmosphere or earth from the bombardment of molecules by fast-moving electrons, and gamma rays result from the natural disintegration of radio-active elements. Cosmic rays come, so far as known, only from interstellar space.

All wave-lengths of radiant energy can be transformed into other forms of energy and can affect material bodies. But because nothing is yet known of the effect on the human body of some of the fractions of radiant energy, discussion will be limited to infra-red, visible light, ultra-violet, *x*-ray and gamma ray frequencies.

Infra-red.—The infra-red is an expression of heat radiation from a body. It is a transformation of heat in the form of radiant energy as contrasted to the transportation of heat itself by molecular conduction and convection. When infra-red energies are absorbed by a body they are reconverted into heat.

Every body possessing temperature emits radiant heat energy, but unless the temperature is over 100° C. the energy is of such low intensity as to be detectable only by a special kind of apparatus. It is only as the wave-lengths approximate those of the red rays in the visible spectrum that the human body can feel their effects.

The short infra-red rays are most abundant in solar radiation, but they can be produced in intensive amounts by many varieties of infra-red generators which operate by raising the temperature of metals to a red glow, or near red-heat. This low heat of 100° to 400° C. is obtained by passing electric currents at variable degrees of resistance through carbon arcs or heated coils, plates and bars. They produce radiations with wave-lengths of from 800 mμ to 5000 mμ.

According to Laurens,[1] the infra-red rays make up 52 to 60 per cent of the total radiation intensity of sunlight when the sun is moderately high. Spring sunlight is strongest and richest in infra-red. The same author states that the percentile relationship between infra-red and the other wave-lengths is variable and dependent on atmospheric density, temperature, humidity, circulation, time of day or year, latitude, and altitude.

[1] Laurens, H: The Physiological Effects of Radiant Energy, Chem Cat. Company, 1933

The penetrability of infra-red rays into the tissues of the human body *depends in great part on their wave-lengths, the shortest* lengths being able to penetrate most deeply. The depth to which they can pass is also dependent on the type of tissue.

The most penetrating infra-red wave-lengths are those between *720 mμ and 1400 mμ. They are said to penetrate subcutaneous tissues* to a distance of 10 to 30 mm.[1] The skin has little absorbing effect on these rays. Longer frequencies (over 1500 mμ) probably cannot penetrate more than 3 mm.

Since solar radiation contains all of the wave-lengths of the near infra-red series it is an efficient practical source of these rays. The only drawback to their use is their inconstant amount throughout the day and the readiness with which their amount and intensity *may be affected by meteorologic conditions.* There are said to be not more than three or four hours around high noon under favorable atmospheric conditions when they are present in sufficient amounts to be useful. Moreover, they are not concentrated, and this makes it necessary to expose large areas of the body at one time.

Visible Light.—White light from any source contains all wave-lengths from 770 mμ to 400 mμ. When dispersed through a prism or grating they show as bands of color. These colors in the order of their increasing frequency (decreasing wave-lengths) are red, orange, yellow, green, blue, indigo and violet.

They have little power of penetration through human tissues and make themselves felt only because of the sense of heat they produce by the absorption of some of the heat rays at the red end of the spectrum. Most of the effects commonly attributed to bright lights such as Klieg lights, electric arcs, sun-gazing, etc., are not due to their visible rays, but the ultra-violet radiations which accompany them (*vide infra*).

Ultra-violet.—Although all wave-lengths of less than approximately 400 mμ are "beyond the violet" of the visible spectrum, the term ultra-violet is now limited to those frequencies lying between the visual violet and the "soft" or long wave-length *x*-rays (50 mμ according to some authorities and 12 mμ according to others).

Sunshine (solar radiation) probably never contains wave-lengths less than 290 mμ, even under the best atmospheric conditions. This limits natural ultra-violet radiation on the earth from this source *to less than one-half of its total possible wave-lengths. The measure*ments and effects of the rays between 300 mμ and 50 mμ (or 12 mμ) have been made on rays artificially produced.

Ultra-violet intensity at the level of the earth is highly susceptible to the physical state of the air above. Passing clouds, dust particles, and water-vapor are all capable of reducing the amount of ultra-

[1] Kovács, R.: Electrotherapy and the Elements of Light Therapy, Philadelphia, Lea & Febiger, 1938.

violet reaching the ground. Of great importance to life in general is the shielding effect of ozone in the upper trophosphere. Ozone has an absorption band at about 250 mμ and to this is attributed the natural limitation of solar radiation to approximately this figure. Humphreys[1] believes that without the protecting layer of ozone ultra-violet radiations down to 200 mμ at least would reach the earth and be destructive to many organisms.

The ultra-violet intensity is also influenced by variations in the amount emitted from the sun, the distance of the sun from the earth, the sun's altitude, and the sun's zenith distance.

Laurens states that the ultra-violet in the light of the setting sun diminishes at the expense of the infra-red. Seasonal variations are marked throughout the world, the total ultra-violet being generally 5.04 times greater in summer than in winter. Laurens shows a difference in the long and short ultra-violet rays in this respect, stating that in contrast to the above figure the short ultra-violet is 15.59 times greater in summer than in winter.

Artificial sources of large amounts of ultra-violet rays are of two main types; the flaming carbon arc, with or without the admixture of a metal or metallic core in the carbon, and the arc produced by an electric current passed through vaporized mercury, tungsten, or iron in a partial vacuum. Although all of these sources emit rays in the ultra-violet, visible and infra-red spectrum, the proportions of these components are variable. The carbon arc most resembles the natural sunlight spectrum. The radiations from ultra-violet lamps can be limited to desired wave-lengths by the use of filters. For a complete discussion of the available types of lamps, the physical properties and penetrability of their rays, the voltage, amperage and distances at which they are to be operated, and the varieties and physical properties of the glasses and filters to be used in conjunction with them the reader is referred to standard works on ultra-violet light and light therapy.

Ultra-violet rays are quickly absorbed by protoplasm and on the human are barely able to penetrate the most superficial layers of the skin. Most are absorbed by passage through 0.1 to 0.3 mm. of skin, although some of the longer wave-lengths near the visible spectrum may penetrate as far as 2 mm.

The human cornea absorbs all wave-lengths shorter than 295 mμ and the lens is opaque to radiations of less than 306 mμ (Laurens).

X-rays (Roentgen Rays).—*X*-rays are probably produced in the intense heat of the sun and the interior of hot stars but never reach the earth in appreciable quantities. It is theoretically conceivable that they may be formed on the earth under exceptional circumstances.

[1] Humphreys, W. J. Bull Nat Res Counc, 61, 98, 1927.

The only source from which they originate in quantities to affect man is the Crooks tube or x-ray tube, in which cathode rays are *made to impinge on a metal plate in a vacuum. The electronic* bombardment disrupts the electron arrangements within the atoms of the metal and liberates radiant energies with wave-lengths of the order of 50 mμ to 0.01 mμ.

X-rays are penetrating to material substances in proportion to *the density of the substance. They are least penetrable through* lead. They can penetrate all parts of the human body, even the bones being able to absorb but a few of them.

Gamma Rays.—These are spoken of by some as high frequency x-rays in the same way that x-rays may be short-wave ultra-violet *rays. They are emitted in the spontaneous degeneration of radio*active substances such as radium, thorium and uranium. Their frequencies are very rapid with wave-lengths of less than 0.01 mμ.

Due to their rapid vibration and high energy they can penetrate deeply into human tissues. The only artificial source of gamma *rays is from the experimental transmutation of elements brought* about by bombarding them with electrons whose speed has been stepped up by high-voltage currents. The number and duration of the rays so produced is too insignificant to permit observation of their effect on the human body.

The Effects of Radiant Energy.—*When evolutionary changes* occurred in man in the past, they took place under his exposure to solar radiation of varying intensities, and possibly, extent. Irrespective of the wave-lengths which impinged on his body they must have affected his skin and eyes most directly. This does not pre*clude the possibility that the more penetrating rays of the spectrum* might have affected other tissues and organs, but these could only have been reached directly or indirectly by way of the skin and cornea. The racial pigmentation of the skin is an inherited characteristic and varies from the near-black of the true negro to the fair pink of the Caucasian. It is assumed to be due to the gradual adaptation of these races to the solar spectrum intensities in the areas where they developed. The theory implies that the pigmentation is a protective response to harmful rays and possesses survival value because it protects the whole organism. On the other hand, there is no evidence that any parallel protecting mechanism has been developed for the eye. The corneal and lenticular tissues stop rays of the same wave-lengths in all races. It is possible, however, that the dark eyelids and dark irises of the colored races may protect the eye somewhat by dispersing and reflecting rays at the pupillary opening.

The pigment of the skin is melanin, an organic colloid produced extracellularly in the acquired types of pigmentation but appearing *intracellularly in the negro skin. In acquired types melanin is*

formed by the activation of tyrosinase (an enzyme) by the light rays. Tyrosinase is converted into tyrosin, and then through an intermediate product, dioxyphenylalanin (dopa), into melanin. The melanin is found only in the basal layers of the skin. Pigment granules in chromatophores are phagocytized melanin. Melanin absorbs all wave-lengths of solar radiation and converts them into heat. Laurens describes these granules as "innumerable little collections of heat energy." They act like black bodies by converting harmful rays into heat. The heat is then passed on slowly to the tissues and circulation and is readily accommodated by the heat regulatory mechanisms of the body.

The superficial layers of the epithelium, those which are "outside" the melanin, have no such protection. When ultra-violet light of high or long continued intensity strikes the horny layers of the skin it produces colloidal changes in the cells which lead to swelling, and later, thickening and keratinization. This more opaque, thickened layer now reflects and disperses more rays than formerly and consequently absorbs fewer of them. Many observers claim that the thickness of the superficial epithelium is the most important single factor in determining the resistance to sunburn and that the most susceptible parts of the body are those where the epithelium is thinnest.

Before considering the effects of specific wave-lengths on the different functions of the body it will be necessary to refer to some general opinions on the effect of radiant energy on living protoplasm and the human organism as a whole.

The following quotations from Laurens'[1] extensive review of the subject and his interpretations are selected as representing the most recent authoritative generalizations on the mechanisms of cell and tissue response to radiant energy:

"The effect of radiation of a given wave-length is directly proportional to the coefficient of absorption of protoplasm for that wave-length. All radiation transfers energy to molecules which absorb it and produce heat, but certain frequencies fall in step with the oscillation periods which depend on the molecular structure and so break up the molecule when the energy absorbed is sufficient."

"Irradiation with the wave-lengths that we are interested in (infra-red, visible light, ultra-violet) has two effects, stimulative and lethal. In general, the first is exerted by wave-lengths to as short as about 290 mμ, the second by those shorter, perhaps by the production of a toxic photo-product, which in small quantity may act as a stimulant to cell division. Put another way, it may be said that the longer ultra-violet rays between 400 and 300 mμ do not

[1] Laurens, H.: The Physiological Effects of Radiant Energy, Reinhold Publishing Corporation, 1933.

produce the marked effects obtained from those shorter than 300 mμ. In the action of radiation we have two elements, a photo-chemical and a biological one. The photo-chemical effect ends with the production of the dermatitis and the activation of substances in the skin and possibly in the blood, while the biological, the effect on metabolism, growth, circulation, etc., lasts for some time."

"The only reasonable conclusion (to the argument as to whether ultra-violet light could act directly on deep seated organs) is that following ultra-violet irradiation some photo-chemical substance formed in the skin is carried by the blood stream to the various organs, there bringing about the observed changes."

"According to Bovie, it is the instability of the physiological mechanism rather than particular wave-lengths which determines the nature of the physiological effect produced, since he and his associates have demonstrated that rays from widely separated regions of the spectrum, provided their ability to penetrate the *organism is such that similar parts are irradiated, produce similar* physiological effects, regardless of the wave-lengths. They postulate, therefore, that the differences observed in physiological effects are due to differences in penetrating powers rather than in any action *specific for wave-lengths. In the visible and ultra-violet regions* absorption depends upon molecular composition, and the roentgen and gamma regions upon the atomic composition of the irradiated protoplasm."

Laurens states in conclusion, "However the action of radiant energy may be explained, granting that the incipient effect is photoelectric, it must be admitted that photochemical reactions ensue, new or changed substances arise in the skin and these passing into the blood produced the variety of effects which have been discussed above."

Roentgen and gamma ray radiations are almost physically identical; the main characteristics which differentiate them are their wave-length and permeability. There is no apparent difference except quantitative, in their action on living tissue.

Although protoplasm is regarded as a chemical entity, the living cell is neither homogeneous, stable nor permanent. The colloidal systems of cytoplasm, nucleus, nuclear and cellular membranes, and the many lesser identifiable parts of the cell are in a constant state of flux which depends on the chemical and physiologic functions of the cell going on at any one time. The short wave-lengths of roentgen and gamma rays enter the atomic structures of these chemical substances and disturb their equilibrium by displacing electrons. The new electron arrangements and the energies released by their shift within the atom will result in new chemical and physical adjustments in the physiology of the cell. Just as gross physical forces

disrupt tissue morphology so these powerful short wave energies disrupt atomic and inter-atomic relationships. The effect on the cell must depend, therefore, on the chemical-physical state of the cell at the time and the intensity and dose of the radiation acting on it.

The threshold at which the normal atomic relationships become abnormal must be highly variable. That is, the dosage necessary to produce permanent abnormal changes in a cell must be as indeterminate as the character of the protoplasm, its physical state and functional activity at the time the radiation acts.

Relative sensitivity of different cells and tissues to radiation can mean only the relative degree to which they are affected under equal dosages of radiant energy under their average state of functional activity. When it is said that a tissue of highly differentiated cells is less sensitive than one of less differentiated cells it now means that this is true not because of the differentiation but because of the differences in the rate and degree of the physiologic processes. Undifferentiated cells are highly active in their metabolism and rate of reproduction and a tissue made up of such cells is in a less stable condition than a highly differentiated tissue. Nevertheless undifferentiated cells may be made less active by cold and other factors and when so influenced may be even less sensitive than differentiated cells. On the average, however, the generalization seems to hold and it is possible to create an average scale of sensitivity of tissues. Desjardins'[1] relative sensitivity table may be reduced to the following arrangement of general types of cells in decreasing order of sensitiveness: lymphocytes, leukocytes, epithelial cells, connective tissue cells, muscle cells, bone cells, fat cells and nerve cells.

The physiologic changes brought about range from inconsequential temporary disturbances from which recovery is rapid and complete to progressive irreversible reactions which terminate in death. The changes are therefore so numerous as to prohibit any detailed discussion of them in this work. In general they differ qualitatively in no wise from those brought about by other physical agents such as cold and heat. The terminal event is always necrosis. Some discussion centers around the question whether these short wavelengths ever stimulate cells, but the general consensus of opinion is in the negative on the assumption that any apparent stimulation is indirectly the result of increased activity following varying degrees of destruction.

As with the radiant energies previously considered the general opinion is that there is no specific wave-length effect. As a result the action of roentgen and gamma rays is identical, but their effectiveness is a function of their penetrability. The degree of

[1] Desjardins, A. U.: Am. Jour. Roentgenol., 32, 493, 1934.

their effect on the cells is determined therefore by the accessibility of the cells and the quantity (dosage) of the irradiation employed.

From the foregoing statements on the effects of radiant energy on protoplasm and living cells in general it is evident that their effects on specific cells and tissues in the human must be conditioned by several important factors. First among them is the accessibility of given cells to given wave-lengths. Ignoring indirect effects for the moment, a cell which cannot be reached directly by a penetrating ray cannot be affected by it. For example, visible light rays cannot reach the medulla of long bones and therefore have no direct action on it, while x-rays can pass completely through *the medullary canal and affect it. On the other hand, heat rays* can exert themselves on cells well embedded in subcutaneous tissues, while the shorter ultra-violet waves are stopped by melanin in the basal layers of the skin.

Since radiant energy is a primary categorical factor in the cause of disease, and the abnormal states which it brings about depends to so great an extent on the tissues and organs affected, these tissue responses will be briefly reviewed.

In considering special tissue effects it must be remembered that some of the changes are due directly to the action of the rays, while others are secondary and result from a chain of physiologic or *pathologic alterations.*

Solar radiation impinging on the skin produces photothermal reactions through the long red and infra-red rays and photo-chemical changes by the short and medium wave-lengths in the ultra-violet. The first raises the temperature of the skin, sweat glands, intracapillary blood and subcutaneous tissues by the liberation of heat. The direct result is therefore local elevation of temperature. Following this reflex, capillary dilatation takes place which increases the amount of blood to the part, stimulates sweat gland activity, alters the osmotic balance between tissue fluids, and brings more fluid and cellular elements of the blood into the field. Still more remote effects are reflex changes in other parts of the body, and the influence of the added quanta of heat energy carried to all *tissues through the blood stream. The local picture of the com*bined effects is increased heat, redness and swelling, *i. e.*, erythema.

The ultra-violet range of the spectrum acts directly only on the outermost layers of the skin. If it is an exposure on a relatively unpigmented skin the short rays penetrate to the basal layers and stimulate the formation of melanin. On the superficial layer it *produces chemical changes in the cells as it passes through them.* These changes, largely colloidal in nature, cause swelling of the protoplasm and therefore thickening of the outer layers. Due to the combined effect of melanin and thickened, more opaque cells, less and less ultra-violet light can get beyond the basal layers.

Continued exposure increases the amount of melanin and brings on the appearance of tanning. If the initial exposure is very intense the cells of all layers of the skin undergo chemical changes to an intolerable degree, and necrosis results. In severe sunburn the necrosis is manifested by blisters and all of the phenomena of an ordinary heat burn. Peeling is a delayed shedding of necrosed epithelium which has been brought on by more moderate exposures. In addition to the visible changes there are remote effects probably brought about by the development of abnormal chemical constituents originating from broken-down proteins. One of these is probably a histamin-like substance. Fever, headache and the unconsciousness of sunstroke are evidences of such disturbances in distant body functions.

The picture of sunburn is completed when to the combined photo-thermal and photo-chemical effects are added the subjective symptoms of burning, tenderness of the skin, stiffness of joints when they are involved, and secondary malaise, anorexia, sleeplessness, and other psychic manifestations.

The activation of ergosterol in the deeper layers of the skin by ultra-violet light may be considered as a special tissue effect of radiant energy. For a discussion of this effect the reader is referred to the section on vitamin D (p. 110) and below (p. 370) in this section.

The conjunctiva and superficial structures of the eye are affected by all wave-lengths which affect the skin. The hyperemia, swelling, sense of "sand-in-the-eye," and later, purulent discharge, are evidences largely of photo-thermal effects of visible and infra-red light plus some degree of cell damage brought about by the ultra-violet rays. When the exposure has been intense the swelling of the cells, especially those of the cornea, may go on to necrosis and end in corneal ulceration and opacity.

There is much controversy over the influence of strong light of all wave-lengths on the deeper structures of the eye. In a review of the literature to date one is impressed with the lack of unanimity of opinion, and this seems to arise from lack of information on the physiology of the refracting media. The lens is complex in structure and apparently also in physiology as evidenced by the studies on the biochemistry of its different parts. All workers agree, however, that the effect of thermal and chemical rays are conditioned more by their intensity than their specific wave-lengths. Sunshine, sky shine, the glare from snow and sand, and the variable spectrum from molten glass and metals, as well as the radiations from arc and mercury vapor lamps are complexes of energies, and if intense enough and of sufficient dosage, are all capable of injuring one or more parts of the eye. It is sufficient to say that visible and invisible light intensities are capable of producing everything from simple

physiologic fatigue to severe destructive processes in the cornea, lens, ciliary body and retina.

Glass blowers' cataract has been linked up largely with excess of the heat-producing rays, and senile cataract with the ultra-violet plus a modicum of heat effect from the visible and infra-red. Snow and sand blindness are believed to result from the concentrated ultra-violet radiations refracted and reflected from these expansive white surfaces. Eclipse scotoma, following exposure of short duration is, on the other hand, presumed to be an intense power burn.

Ultra-violet rays from wide sources such as sunshine and sky shine are believed to exhaust the visual purple of the retina in the absence of sufficient vitamin D and lead to functional blindness.

The influence of irradiation on the circulatory system is primarily a reduction of blood-pressure. Under experimental conditions the lowered pressure is slight and transitory, and there is no evidence that it is a factor of any permanent significance under ordinary conditions of exposure to sunlight. According to Laurens, "The factors held responsible are diverse, namely, cutaneous hyperemia; changes in blood viscosity; the production in the skin of depressor substances which, getting into the blood stream, lower the peripheral resistance; the breathing of depressor substances, such as oxides of nitrogen and similar compounds set free by the arc; sympathetic hypotonia, and perhaps others." Whatever their nature, the changes are within the limits of physiologic tolerance and it seems unlikely that irradiation in health can result in disease through its action on the circulatory mechanism *per se*.

Most of the data reported on the effect of irradiation on the formed elements of the blood were obtained under conditions which preclude any comparison of the studies and their results. In order to get specific results Laurens, Mayerson and their co-workers studied the effects of known wave-lengths on dogs under controlled experimental conditions of diet, exposure to light, blood volume, etc. As a result of their studies, the following brief statements can be made about the effects of the "pan-ray" and "sunshine" carbon arcs on dogs: a gradual increase in erythrocytes after the cessation of irradiation (sixty minutes every other day for two weeks) to twice their pre-irradiation number; a parallel increase in reticulocytes; persistent low hematocrit value and therefore decreasing corpuscular volume; insignificant changes in hemoglobin or corpuscular saturation.

There is little question that irradiation causes a leukocytosis with a predominant increase in the lymphocytes.

Immediately after irradiation there is a lowering of blood serum and calcium which Mayerson[1] explains as due to dilution of the blood by its increase in volume following the absorption of tissue

[1] Mayerson, H. S.: Amer. Jour. Physiol., 81, 686, 1927.

fluids from hyperemic areas. Laurens believes that all of the reports showing reduction of red cells and hemoglobin after irradiation can be explained on the basis of increased plasma volume.

Although much has been written on the influence of irradiation on diseased states there is little to be said on its effects on the normal and whether it can or cannot produce disease in normal individuals. Mayerson, Gunther and Laurens[1] (1926) undertook the study of metabolic changes occurring in dogs following irradiation, and in dogs living in darkness which were brought into sunlight and *vice versa*. In the first instance they found that moderate intensities of Sunshine Carbon Arc irradiation increased the endogenous nitrogen metabolism, stimulated the absorption of calcium and phosphorus from the intestine, and decreased the amount of blood sugar. Laurens summarizes the findings in dogs brought from darkness to sunlight and from sunlight to darkness by saying that in both cases there was a stimulation of endogenous nitrogen metabolism and changes in the partition of calcium and phosphorus in the urine and feces, with phosphorus retention He assumes that probably any deviation from the usual, insofar as radiant energy is concerned, acts as a stimulus which disturbs the metabolism of these constituents.

A number of disease states present evidence that in susceptible individuals, radiant energies (especially the ultra-violet radiations) may bring about a state of hypersensitiveness to them. Thus Duke holds that the ultra-violet rays of sunlight produce in some people cutaneous phenomena which are clinically indistinguishable from those caused by organic allergens. Moreover, some patients on exposure to sunlight develop even more general and deep-seated pathology simulating asthma and hay fever. It is not uncommon for some people to sneeze repeatedly on first coming into bright sunshine. A probable link-up between Duke's physical allergy due to sunshine and hypersensitiveness in general may rest on the basis of histamin-like allergens produced in the skin by sunlight on the one hand and by a number of organic agents in different tissues of the body on the other.

In another group of sensitizations are those conditions in which certain photosensitive chemical substances are assumed to be present in abnormal amounts in the skin or in which photosensitive chemicals normally present are activated with undue facility by exposure of the body to sunlight. Hydroa vacciniformis is a disease in which hematoporphyrin and its derivatives uroporphyrin and coproporphyrin are demonstrable in the skin, urine and feces. These substances are all fluorescent in ultra-violet light. The seasonal incidence of hydroa vacciniformis in the summer and its aggravation

[1] Mayerson, H. S., Gunther, L., and Laurens, H. Am Jour. Physiol., 75, 399, 1926.

at times by snow-glare in the winter point firmly toward its connection with light intensity. Moreover, hematoporphyrin is the only natural fluorescent substance known in the body.

Xeroderma pigmentosa (Kaposi's disease) is a tendency to massive freckling, severe sunburn, keratosis, atrophy of the skin, depigmentation, and malignancy of the skin. It is of familial occurrence but not definitely proven to be hereditary. Although it is not assumed that actinic rays of sunlight cause the disease there is no doubt that ultra-violet, and possibly visible rays, are the important activating agents. The true nature of the susceptibility to these radiations is not known.

Sunlight is said by some to be a factor in the production of cancer of the lower lip. It is postulated that the excessive exposure of the lower lip in persons whose lower lip is large and everted results in photo-chemical and photo-thermal changes conducive to carcinoma.

For many years the symmetrical distribution of the cutaneous lesions of pellagra has been explained on a photo-dynamic basis. No definite evidence has been brought forward in support of the theory but it is not improbable that some photosensitive reaction may be found to underlie the remarkable distribution of the lesions on the exposed wrists and neck.

X-rays and radium are unquestionably carcinogenic. (In the case of radium consideration must be given to the part played by its alpha and beta emanations as well as its gamma rays.) The close correlation between the malignancies developing in the epithelial tissues following *x*-ray burns or the slow epithelial changes from often repeated exposures to rays of low intensity and dosage, and the carcinomatous changes produced by experimental irradiation with roentgen and gamma rays leaves little doubt as to the causal relationship between them. The mechanism by which malignant change is brought about must remain in doubt until more is known of the nature of malignancy in general.

Clinical observation long ago revealed a selective destruction by roentgen and gamma rays of the cellular elements of the gonads which leads to sterility in both sexes. This has been experimentally confirmed and the principle is now applied in producing artificial sterility for therapeutic or legal purposes.

In concluding the discussion of radiant energy a word must be said regarding the usefulness of the whole effective range of the electromagnetic spectrum on the entire human organism. It is probable that the human could live without light provided all other environmental factors necessary for growth and development were present. But this does not imply that he would ever reach optimum efficiency. The close relationship between man's physical and chemical constitution and the physical and chemical properties of his light environment make it appear that his normal physiologic

equilibrium is largely conditioned by light. Even this brief review of the effect of radiant energy on metabolism reveals important shifts in electrolyte balances which may be necessary to keep up the state of relative equilibrium of the body as a whole; that without the constant flux brought about by a shifting environment, the necessary stimuli to internal readjustments would be lacking and a lethal inactivity result. The science of the human organism is nowhere near the point where the effect of the entire light environment on the whole organism can be determined by studying the effects of the isolated components of the spectrum on the isolated functions of the body. Nor is the radiant energy spectrum to be isolated from other environmental factors. It may be true that certain intensities and dosages of specific wave-lengths may bring about specific results, but health is maintained by the phylogenic inheritance of an organization able to adapt itself to them and in so doing benefit from the conflict. Sunlight itself cannot sustain life without the necessary nutritive elements, nor can these two maintain health without the support of all other environmental factors. Categorically radiant energies can produce disease through their effects alone, but they are only one element among inheritance, atmosphere, food, parasitesand biosocial factors that go to produce a healthy man.

CHAPTER XXXVI.

THE DEFENSE AGAINST RADIANT ENERGY.

THE practice of overexposing the body to sunlight has become popularized on the assumption that tanning of the skin is synonymous with health. Tanning is a natural defense mechanism, limited to the skin on the anatomic side and to protection against the deep effects of ultra-violet rays on the physiologic. But it must be emphasized that the photo-thermal rays are not stopped by melanin and the photo-chemical rays are absorbed in the epidermis only by virtue of pathologic changes induced in the superficial cell layers of the skin.

Insolation reactions can therefore occur, though less readily, through pigmented skin. Since the ability to produce melanin under the action of ultra-violet light is highly variable among individuals it follows that any generalization about the amount of exposure must be so qualified as to lose its significance entirely. In a beach full of bathers some will tan quickly and others hardly at all; some will feel no more than a pleasant glowing reaction and others will become confined to bed with severe sunburn and general body reactions.

Whereas a certain amount of surface erythema might be beneficial in improving the skin circulation there is no evidence that sunburn is of any value in health. Tanning is taken by some as an index of the curative properties of light in the treatment of tuberculosis, although it is not at all certain that this belief is well founded. On the other hand, repeated heavy exposures on a skin which will not tan is undoubtedly harmful. The local and general thermal disturbances and the liberation of split-protein products into the circulation may be the cause of unforeseen derangements in the metabolic functions of internal organs—liver, pancreas, brain, thyroid, parathyroids, bones, etc.

On general principles it may safely be said that it is at least unwise to overexpose the body to direct sunlight. Short periods do no harm if painful sunburn does not result, especially in dark-skinned individuals or those who have become tanned. Blondes pigment with difficulty and should be especially cautious.

Similar reasoning, with still greater justification can be applied against the home use of artificial radiant heat and ultra-violet light. In addition to the skin effect there is always the danger of damage to the eyes. The exorbitant claims of therapeutic lamp manufac-

turers have led to the use of these appliances for purposes far beyond their powers. They have some therapeutic value on which their use is entirely justified, but they should be used only on the advice of a competent physician who understands the nature of their effect and can intelligently direct the patient as to the frequency and length of exposure, amount of current, distance from the lamp, types of filters, and general precautions in their use.

When prolonged exposure to sunlight is unavoidable the skin should be protected by light clothing or, when this is impractical, the skin should be rubbed with a light oil or vaseline to help absorb the rays. This is especially true when wetting of the body occurs during the time of exposure, for wet skin burns more readily.

Individuals differ in the sensitivity of their eyes to the visible rays of sunlight. This is probably explained on the physiologic level and does not necessarily connote disease. It does, however, imply eye fatigue and results in some degree of photophobia, lachrymation, painful orbits, and headache. Such persons should habitually wear tinted or smoked glasses to cut down the intensity of the visible light.

Under certain circumstances and in some occupations exposure to harmful intensities of ultra-violet light is unavoidable. Mention has already been made of snow and sand blindness. Eyeshades to to cut down the source of these rays and special filter lenses to reduce the ultra-violet are indicated in all occupations where the worker must face bright incandescent lights. Electric arc welders, glass workers, operators of ultra-violet light generators, incandescent lamp manufacturers and workers, carbon arc machine operators, moving picture actors who must face brilliant floodlights, should all protect their eyes by suitable goggles or glasses whenever practicable. No one should ever attempt to look directly at the sun when it is bright, and during an eclipse should do so only through smoked or darkened glass.

Deficiency in the amount and intensity of ultra-violet light may be a factor in the development of rickets, and for this reason it may be necessary to supplement it by artificial means. Ultra-violet light does not take the place of vitamin D, calcium or phosphorus in the food, but augments the activity of the first and regulates the distribution of the two latter elements. With this qualification, a lessened amount of ultra-violet light may be looked upon as a cause of disease.

Although the prevalence of clinical rickets is on the decline there is probably a high incidence of this disease in its subclinical stage. Infants reared in close, poorly-lit and ill-ventilated surroundings undoubtedly get insufficient ultra-violet light, and although their diets may now be better than in the past they lack this essential stimulus to calcium and phosphorus metabolism. The prevention

of rickets is therefore largely one of supplying an adequate amount of ultra-violet light. This is of special importance in industrial centers where the air contains a large amount of dust and smoke particles. It is also generally true of most localities in the winter when the ultra-violet intensities are greatly reduced.

Children brought up under these circumstances should be exposed to the sunlight daily. In institutions they should be placed in solaria which are open in the summer and closed in winter behind synthetic glass which is made to permit the passage of ultra-violet light. When natural sunlight is not available in sufficient quantities resort may be had to the use of artificial sources such as the quartz mercury vapor lamp. The dosage and distance of the lamp must be regulated and used under competent supervision and the children's eyes must be adequately protected.

Protection from roentgen irradiation is dependent on three principles: (1) Avoidance of exposure; (2) the use of screens and filters; (3) focusing of the rays.

In following the first, operators of *x*-ray machines must understand that nearness to the machine is commensurate with exposure. Scattering of rays and secondary emanations always occur and cannot be avoided by any one in close proximity to the machine. Although the dosage at any one exposure may be minimal, there is danger from repeated small doses. The tubes should never be adjusted after the current has been turned on and the actual operation of the machine should be performed at a control board well removed from the *x*-ray outfit itself.

Attendants on *x*-ray machines should have four consecutive weeks out of a year of complete removal from exposure to *x*-ray emanations.

Screens of lead should separate the control room from the *x*-ray machine. Lead-impregnated aprons and gloves should be worn while operating the fluoroscope or attending patients under the rays.

The newer *x*-ray tubes and machines have improved the protection to attendants and operators by being enclosed in materials impenetrable to the *x*-rays. Scattering and secondary emanations have been reduced by confining the exit of the rays to a small aperture directed toward the object to be exposed.

CHAPTER XXXVII.

THE EFFECT OF ELECTRICITY AND ELECTRONIC FORCES.

The Electron Theory of Matter makes it possible to explain many of the divergent phenomena of electrical, chemical and physical change on the single basis of electronic forces and energies. By this theory much has been accomplished to explain the mode of action of electrical and electronic forces on the body. The fundamental conception is the possession in common by electricity and protoplasm of electrically charged particles (accepting the particle theory as a working basis) which are similar in nature and energies and therefore interchangeable. Free-moving electrons of an electric current passing through protoplasm can enter into the atoms of the protoplasmic elements. The addition to or subtraction of electrons from atoms changes the ratio between the negative charges (electrons) and the positive charges (nuclear protons) and brings about a change in the charge of the atom as a whole, alters its mass and releases energy. The energy released may be converted into thermal, mechanical or radiant forms, and so bring about the familiar reaction of chemical and physical change.

The normal physiology of the cell being largely concerned with the activities of charged particles (free electrons, atoms and molecules) it is readily understood how electric forces brought into the body from the outside can augment, neutralize or overwhelm these normal minute charges of electricity.

If the external electrical force is of such nature as to augment intracellular and intercellular electrical reactions, it results in stimulation of the cellular functions concerned. On the other hand, antagonistic forces can bring about changes of such serious nature as to cause suppression of important functions and lead to disintegration of cells and tissues and terminate in necrosis and death.

The conversion of the electrical energies into heat, light, radiant energy and mechanical force may also augment or oppose normal *mechanisms and bring about similar results.*

All of the factors which are concerned in the conduction of electricity and its conversion into other forms of energy in non-living conductors are also of importance in the living body. Thus, the effect of any electric current or field of force on the body will be determined by the conductivity and resistance (ohms) of the tissues which are concerned and the force of the current (voltage), rate of work (watts), rate of flow of current (amperage), type of current,

whether direct (continuous) or alternating, and in the latter, the rate of alternation (cycles).

The forms of electrical energy to be considered under this category are: lightning, artificially produced electric currents, electrostatic charges, and emanations from radioactive substances (other than gamma rays, for which see under Radiant Energy, page 359).

Lightning.—The lightning discharge has an electromotive force of high voltage, reaching probably some millions of volts. It is a direct current discharge between the high potential charge on the clouds and the low potential on the earth. In its passage across this gradient it meets at times with the human body, which acts as a conductor. More or less of the entire discharge may pass through the body and either be stored on it as a temporary static charge or run off by some other conductor. The resistance varies with the tissues of the body concerned and the degree of insulation of the body from the conductor on which it rests. The lightning current acts in three ways to cause damage to the tissues: (1) By the production of high temperatures by its conversion into heat; (2) by electrolytic action; (3) by mechanical force brought about by the repulsion between tissue particles bearing the same electrical charge.

When a person who is poorly insulated from the ground is struck by lightning the current is run off rapidly to the ground. Most of the current passes across the surface of the body and does little harm. Wherever it meets with high resistance, as from excess moisture in wrinkles and folds of the skin, it is converted into heat and produces burns. For the same reason metal objects on the body or carried in the hands or pockets cause localized burns. The current through the body probably passes largely by way of the blood-vessels because the blood, according to Critchley,[1] is by far the best conductor of all the body tissues. Cerebrospinal fluid is the next best conductor according to the same authority. Many of the phenomena of this type of injury are ascribed by Critchley to primary vascular changes. The small cerebral hemorrhages appear to be due to the passage of the greater part of the charge through the vessels of the brain, and the bilateral paralysis (keraunoparalysis) is believed by him to be due to vascular spasm analogous to that seen in Raynaud's disease. The same authority is of the opinion that the vascular spasm, electrical edema, cyanosis, pupillary irregularities and whitening of the hair are secondary trophic disturbances resulting from electrical shock to the autonomic nervous system. The familiar lightning streaks seen through the skin and supposedly mirroring the branched lightning flash are generally believed to be spastic blood-vessels.

Postmortem changes in the brain have been difficult to account for. They have been described as vacuolizations, holes, gas pockets,

[1] Critchley, M.: Lancet, 1, 68, 1934.

distended tissue spaces, and separation of tissue layers accompanied by more or less gross hemorrhage. To explain these findings which are peculiar to electric shock it was postulated by Spitzka and Radasch[1] that gases were produced by electrolysis and that the accumulated gases disrupted and distended the tissues. Vaporization of moisture by the heat energy of the electric current has also been thought to explain these findings.

More recently, Pritchard[2] has given the most satisfactory explanation of these changes. Arguing from electrostatics, he has shown that a lightning stroke produces a heavy static surface charge on the skin and that under these conditions every particle of the skin will carry an electric charge of the same sign. Because bodies with like charges repel one another there will be a tendency of the surface particles to fly apart. They are prevented from doing so by their rigidity and cohesion, but the total effect is that of a force acting outwards from the surface. Pritchard has estimated that this force may be equivalent to the sudden reduction of the atmospheric pressure by one-half. This almost instantaneous expansive force will be communicated inward to all tissues within the body and they will, in turn, attempt to expand outwardly. The softest parts will yield first, and separation of tissues with little rigidity and cohesion between them will then take place. The vessels and perivascular tissues, subarachnoid space and cleavage lines between cortical layers of the brain are examples of areas of low cohesion and are the places where the postmortem findings described are most frequently seen. Small hemorrhages result in these areas from the tearing of cerebral and meningeal vessels.

Cerebral trauma is most likely to occur when the cranium is one of the terminals of the current. When other parts of the body are struck first, the central nervous system is often little, if at all affected because of its relatively low coefficient of conductivity. In non-fatal cases with loss of consciousness Critchley states that the cerebral symptoms are probably due to hemorrhage, cerebral edema, elevation of brain temperature and "possibly molecular changes of such character as will elude present day forms of detection."

Combinations of thermal, electrolytic and static charge effects seem to explain best the majority of pathologic changes found after lightning stroke. Rapid muscular spasm and widespread injury to the autonomic nervous system are sufficient in themselves to account for the subjective symptoms which have been described by the victims in non-fatal cases and by onlookers. The indefinite term "shock" is thereby put on a more tenable basis, and many of the formerly inexplicable and bizarre happenings are rationally accounted for.

[1] Spitzka, E. A., and Radasch Am. Jour Med Sci., 164, 341, 1912
[2] Pritchard, E. A. B. Lancet, 1, 1163, 1934

Artificial Electric Currents.—The effects of artificial electric currents do not differ fundamentally from those produced by lightning stroke. The main observed differences are due to such conditioning factors as completeness of contact, parts of the body acting as terminals for the circuit, the controlled variation in the strength of the current, duration of contact, rapidity of alternation in alternating currents and to some degree the physiologic state of the body when the contact is made.

The source of the electric current is of great importance because by it the strength and nature of the current is largely determined. The ordinary house circuit varies from 110 to 220 volts and 15 or 30 ampères. In some installations a direct current is used, but more commonly it is alternating, with frequency cycles of from 50 to 60 per second. High tension currents carrying voltages up to 220,000 are generally alternating currents. The rapid frequency d'Arsonval currents with alternations of 750,000 to 3,000,000 per second are used in diathermy.

Power currents vary from 400 to 26,400 volts and currents for street lighting circuits average 2000 to 5000 volts. The circuits for small power units, elevators, etc., are protected by fuses with a capacity of 30 to 50 ampères. When a part of the body comes in contact with an open circuit, provided the body is not otherwise completely insulated, the current enters the point of contact as one terminal and leaves by such other parts as may be in position to complete the circuit. The course which the charge takes through the body depends on the resistance of the tissues which can conduct it and the strength of the current. In general, it may be said that the blood stream offers least resistance and the central nervous system is seldom affected unless the head acts as one of the terminals.

At all points of contact between the surface of the body and a conductor the current generates heat, and if the current is strong and the resistance of the tissues high the heat may be sufficient to produce necrosis. If an arc is formed at the contact, a severe fire burn will result.

An electric burn is generally sharply defined and progressive for some time after the injury. The latter characteristic is attributed to vascular damage in the regions just beyond the limits of the actual burn. All other phenomena connected with electric shock are due to special tissue effects. Muscle spasm may cause grotesque contractions of the body and secondary traumatic injury from falling or being thrown about. Neurologic effects result from damage to myelin sheaths, scattered petechial hemorrhages and, according to Critchley, chromatolysis, fragmentation, and tortuosity of the axons of peripheral nerves. Concussion may be an important element in producing immediate unconsciousness. In the opinion of Critchley,[1]

[1] Critchley, M.: Lancet, 1, 71, 1934.

reduced metabolism only when it was previously abnormally high, and increased the metabolic rate only in subjects with abnormally low rates. They confirmed Dessauer's findings that positive ions produced headache in sensitive individuals and irritation in the nose and throat. They showed subjectively that negative ions had a cooling, relaxing effect.

The indirect effects of ionization in the air may be of more importance to man than any direct physiologic action. Since dust particles, salt crystals and water droplets become charged positively or negatively according to the physical circumstances which they meet in the atmosphere, the number and size of the aggregates so formed may make a great difference in the penetrability of the atmosphere by certain wave-lengths of solar radiation and in the conduction of heat. Furthermore, bacteria in the air may act as nuclei of larger aggregates of molecules and so be influenced in their activity and duration of life and the distance to which they will be carried in moving air. This latter may prove to be of significance in the epidemiology of such air-borne diseases as tuberculosis and diphtheria.

Radio-active Emanations.—A small group of elements with atomic weights of over 200 possess the characteristic in common of undergoing continuous, regular disintegration by the loss from their nuclei of positive and negative electrons. This property of emitting nuclear electrons is termed radio-activity, because the electron particles travel through space with high energies and can effect other material substances with which they come in contact. The positive electrons are called alpha-rays and are positive nuclear electrons of helium. They are given off with a speed of 10,000 to 18,600 miles per second, and can travel 1 to 4 inches through air. They are stopped by an ordinary sheet of paper.

The negative electrons are similar to the cathode rays of the roentgen tube, but when emitted from radio-active sources are called beta-rays. They have a velocity which may approach 0.9 that of light, and possess high penetrating qualities. They can pass through a few millimeters of platinum, but are effectively screened by thin sheets of gold, platinum and lead. (Gamma-rays are electromagnetic rays produced by the impact of beta-rays on matter in the same way that x-rays are liberated by cathode rays striking on the metal target of the roentgen tube.)

Through the loss of nuclear electrons, radio-active substances are continuously losing mass and electric charge which results in a change in atomic weight and number of the element. As a result, new elements are being formed and it has been found that this transmutation of elements is going on through a regular series of elements with progressively lower atomic weights. The loss is a

constant percentage of the number of atoms present, and the "life" of such an element is measured in its half-period, that is, the time in which any amount of the element is reduced by one-half. Uranium has a half-period of 4.67×10^9 years; radium, 1690 years; radium C^1, 10^{-6} seconds. Between these extremes are isotopic forms of uranium and radium with half-time periods of seconds, minutes and days. The final disintegration products of the radio-active elements are isotopes of lead.

Although only the alpha- and beta-rays come within the category of electron forces, it is difficult to separate the effects of these rays on living substances from those of the electromagnetic gamma-rays. Although gamma-ray effects may be obtained alone by suitable alpha- and beta-ray filters, beta-rays are always accompanied by gamma-rays which make the results conflicting. The amounts of each may be measured, however, by electroscopic methods, which makes it possible to estimate their proportionate effects with some assurance of accuracy.

The more stable of the radio-active elements and their ores found in sold form in the earth's crust are uranium, radium and thorium. They are closely allied with the alkaline earths strontium, barium, calcium and magnesium, and are found in largest quantities in pitchblende, carnotite, and uraninite ores. Pitchblende is the most profitable source of radium and is mined in the Belgian Congo, Czechoslovakia and Canada. The radio-active elements in their combined native states are continuously disintegrating, so that their ores and salts are also radio-active. As a result, radium emanations are detectable in large amounts in mines where the ores occur. But because uranium and radium were present in great quantities millions of years ago and were widely distributed in the earth's crust, many soils today retain minute amounts which give off measurable alpha- and beta-rays. At present they are found in mines and caves and deep, closed excavations, such as cellars and pits. Some enter the soil water in a gaseous state (radon, thoron) and appear in the water from mineral springs. Alpha- and beta-rays are also present in the atmosphere and are found concentreated in rain and snow.

The radium of commerce is usually the soluble bromide or insoluble sulphate of radium. Radium emanation, or radon, is a gaseous element formed from radium and is put up in small, hermetically sealed lengths of gold or glass tubes called "seeds."

Because radio-active emanations produce visible light when they strike the retina, radium salts are used as ingredients of luminous paints. Luminous paint consists of small amounts of radium or mesothorium in a base of crystallized zinc sulphide with some copper, manganese and cadmium.

The biologic effect of radium emanations is believed to be pri-

marily a disturbance of the protein-lipoid-water phases of the colloidal system of protoplasm. This is brought about by the electron disturbances and imbalances produced by the energies of the alpha- and beta-rays and the gamma radiations, and the secondary influences of heat and other forms of energy which are liberated.

According to Colwell,[1] the physical damage to the living cell seems to be due to change brought about in the permeability of the cell membrane and alterations in viscosity and surface tension in the protoplasmic elements. The same authority debates the question whether radium emanations stimulate autolysis by increasing the activity of enzymes, and states that the experimental results may be explained as well by the action of the rays on the substrate. Autolysis does occur under their action and may go on to cell destruction.

Mitochondria are highly susceptible to these emanations, and their alteration may result in nuclear changes which are non-lethal but can be transmitted to subsequent division products of the cell. This is believed to be the basis of their malignancy-producing tendencies. Martland[2] states that "The alpha-rays are biologically more destructive than either beta- or gamma-rays, the relation being 10,000 to 100 to 1. Therefore radio-active elements in such small quantities that the beta and gamma radiations are almost negligible still produce, through their alpha radiations, intense physiological effects, if given by mouth or vein."

On the other hand, exposure to radium under conditions in which the emanations must travel through air are more effective through the action of beta- and gamma-rays. This is because the alpha particle meets with many molecules in traversing a short distance in air and is thereby impeded. Martland further states that mesothorium in luminous paint is more toxic than radium because mesothorium emits 5 alpha particles to 4 alpha particles of radium.

Exposure to radium emanations occurs in all forms of radio-active therapy and among handlers of radium applications. Operators in uranium mines may ingest or inhale radiant ore dusts, and those in industries who handle and use luminous paints may take considerable quantities of radio-active salts into their mouths.

Radium for therapeutic purposes is put up in sealed hollow needles of gold, platinum or steel, each needle containing from 1 to 10 mg. of radium; tubes of gold, platinum or monel-metal with 10 to 100 mg. of radium each; plaques of metal spread over with radium and having 1 to 4 sq. cm. surface area; bombs or hollow blocks of lead holding any desired number of radium tubes; and the above mentioned "seeds" of radon (radium emanation). Dosage of radium is determined by focal distance from the part, amount of

[1] Colwell, Hector A: The Method of Action of Radium, Oxford Medical Publications, 1935

[2] Martland, H. S.: Am. Jour. Canc., 15, 2435, 1931.

radium and the length of time of the exposure. Differential dosage of the different rays is obtained by the use of filters. In general, platinum gives increased filtration of beta- and soft gamma-rays, plaques with wax fronts permit more of the beta-rays to come through, and radon seeds give high quantities of alpha-rays.

All exposures to radium, except in those subjected to it for therapeutic purposes, and handlers of the needles and tubes, mean contact with all of the rays of radium in their natural strength and proportion. The unfortunate experiences in the luminous watch-dial industry have added much to the knowledge of chronic radium poisoning. For detailed accounts of these poisonings and the studies resulting from them, the reader is referred to the following original sources: H. S. Martland, Occupational Poisoning in the Manufacture of Luminous Dial Watches, *Journal of the American Medical Association*, **92**, 466–473, February 9, 1929; pp. 552–559, February 16, 1929; a summary of the results of an investigation on the subject of the Office of the Surgeon General, United States Public Health Service, by James P. Leake, *Journal of the American Medical Association*, **98**, 1077–1079, March 26, 1932; and H. S. Martland, *American Journal of Cancer*, **15**, 2435–2516, 1931.

In these poisonings it has been demonstrated that the radium entered by way of the mouth and gastro-intestinal tract. Although all emanations were found present in the dust and atmosphere of the work-rooms they were ineffectual in this form in producing physiologic effects.

Ingested radium, on the other hand, permits the absorption of active radiant matter and its deposit in the osseous skeleton, where it is bound through its affinity for calcium, and in the reticulo-endothelium. Each atom of stored radium acts as a constant source of alpha-, beta- and gamma-rays which bombard the blood-forming organs and osseous tissues. The primary effects are therefore osteitis and anemia.

Martland's (1931) conclusions warrant quotation, for they sum up the present conception of the picture of radium poisoning due to the action of radium deposited in the body tissues, whether this *results from its ingestion, inhalation or intravenous injection*: "*In a* radio-active dial-painter who has, for example, 10 micrograms of radio-active substances deposited as insoluble sulphates in the entire skeleton, there are constantly being ejected about 370,000 space-occupying alpha particles a second. The tremendously disruptive effect of ionization produced by this bombardment causes atomic and molecular disintegration. In time, a hyperplastic, red marrow results due to compensatory stimulation. Such a marrow is characterized by a packing of the marrow spaces with primitive stem cells, which I have interpreted as promyelocytes, proerythroblasts and hemocytoblasts.

"The ability to form cells of the granulocytic series, with the

exception of the eosinophil myelocyte, is lost. As these cells are chiefly extravascular in location, very few immature cells escape into the circulating blood; hence the leukopenia with a tendency toward an agranulocytic blood picture.

"The power to form red cells is retained, but greatly reduced and reverts to an embryonal, megaloblastic type of production. As the formation of the red cells is chiefly intravascular, many immature cells are washed into the blood stream, especially macrocytes. Hence the resemblance of the blood picture to Addisonian anemia. This hyperplastic, irritative, embryonal marrow, I have designated as the first stage of radiation osteitis.

"The process now subsides in patchy areas over the skeleton. A very cellular replacement fibrosis, of an intense inflammatory character develops with numerous eosinophil myelocytes, lymphocytes and plasma cells. Many of the fibroblasts show mitotic figures and hyperchromatism, and these areas can be distinguished from sarcoma only with great difficulty. It is in these areas that sarcoma arises. On account of their wide distribution over the skeleton it is easily seen how multiple primary sarcomas may occur in the same individual. I have called this the second stage of radiation osteitis.

"In the final stage of the process of radiation osteitis the marrow is entirely replaced by an old non-cellular fibroblastic tissue. The bones become soft, partially decalcified, and deforming lesions occur."

The tolerance to radium within the body tissues is generally placed at 10 micrograms throughout the entire skeleton. Martland (1931) takes exception to this high figure on the basis of lack of knowledge regarding the possible effects of lesser amounts in producing other types of malignancy. He thinks that even 0.5 micrograms (as found in some of his cases studied) is dangerous and even much less may be harmful.

It is common practice to inject radio-active substances intravenously for treatment of Hodgkin's disease and leukemia and in performing certain physiologic studies. The warning is given by many authorities that this practice may not be without danger, especially when mesothorium is used.

Because of the presence of large amounts of radio-active ores in pitchblende and cobalt mines, it has been conjectured that this may have a bearing on the incidence of primary carcinoma of the lungs in the workers at the Schneeberg and Joachimthal mines.

The deliberate ingestion of radio-active substances is found in the consumption of allegedly beneficial radiant waters. Many mineral waters claiming to be radio-active actually are so. The radio-active content may be soluble salts of radium or radon gas (radium emanation). Both can occur in natural waters, although

radon is the more common. Soluble salts of radium or thorium are on the market, and are dispensed in vial form (2-ounce bottles, each containing 2 micrograms of radio-active substance) to be added to ordinary drinking water. At least 1 death has been reported[1] from drinking such fortified water. The patient had consumed 1400 bottles of radiant salt (said to be "Radithor") over a period of five years. Examination of all tissues at necropsy revealed 73.66 micrograms of radium in the total body.

Radon spring water is relatively harmless compared to mineral waters containing radium. This is because the emanation is highly unstable when brought into the air, and prohibitive amounts would have to be taken to approach the quantity of radium consumed in radium waters. Martland (1931) is still not sure that even radium emanation handled and ingested as such is harmless, and reiterates that it is his opinion that the normal radio-activity of the human body should not be increased.

[1] Gettler, A. O , and Norris, C Jour Am. Med Assn., 100, 400, 1933

CHAPTER XXXVIII.

THE DEFENSE AGAINST ELECTRIC AND ELECTRONIC FORCES.

THE human body, like any other conductor, can act as a more favorable medium than air for the passage of the current of a lightning discharge from the cloud to the ground. If any precaution can be taken against lightning stroke it can be best expressed by two general statements: "(1) Place yourself in such a position that your body will be a less favorable conductor than objects around you; (2) if you are near another conductor keep at a distance of at least a few feet from it." The reason for the first is self-explanatory. The second precaution rests on the fact that if the body is in contact with or close to another conductor which is struck, some of the charge will accumulate on the body and the repulsion of the two charges will throw the body away from the conductor forcibly enough to inflict injuries in addition to those which might result from the electric shock itself. Practically it is unwise to cross a wide open space such as a field during an electric storm. The body is then the only conductor extending above the level of the ground.

There is probably little, if any, truth in the danger ascribed to sitting in draughts or holding scissors and other metal objects in the hands on the basis that they attract lightning. On the other hand, metal objects on the body will tend to increase the damage from heat burns if the body is struck.

The danger from lightning while in swimming is the same as in crossing an open field. This is especially true if the feet are resting on the bottom at the time.

Under most conditions then it is best during a thunder storm to seek shelter near a tree, shed, house, or other conductor, but at the same time remain some 5 or 6 feet from it and not to rest against any small supports or hold any large metallic articles in the hand.

Artificial electric currents from small batteries and dynamos are seldom dangerous, but may produce frightening shocks and mild burns if sparking occurs. No one unfamiliar with the fundamentals of electric currents and principles of insulation should be free with their handling of storage batteries and dynamos such as are used for small lighting circuits. Manufacturers have seen to it in most instances that the most dangerous parts of such installations are

covered and that all switches and contacts are insulated as far as practicable. Children especially should be warned to keep away from such apparatus. All house currents must be considered potentially dangerous, if not lethal. Deaths have occurred from even less than the customary 110 volt alternating circuit for reasons stated in the previous section. This applies not only to the lighting circuit but to all appliances operating on and carrying that circuit.

The danger becomes manifest whenever the current is short-circuited, and this may occur under a great variety of conditions. The short-circuit discharge is usually momentary because protective fuses are placed in the circuit which automatically disrupt it when the short-circuit occurs. Nevertheless, a full charge through the body at the right physiologic moment has produced death.

Short circuits may result from faulty wall-plugs (wall sockets, outlets, etc.), metal objects inserted into empty sockets (babies and children do this) contact with a water faucet or toilet chain with one hand while turning out a light with the other, turning the light on or off with wet hands, contact with open wires in faultily constructed or worn electric household appliances, defective electric warming pads or wet ones, home light-therapy machines, worn insulations or wiring circuits in walls, lighting fixtures, etc., and far too commonly from inexperienced handling in the installation and repair of house wiring and electric appliances without the simple precaution of first throwing the switch at the circuit control box. Children can be taught the simple precaution necessary to prevent such accidents, and adults should have high respect for the dangers of short-circuits.

Under general measures come such precautionary regulations as control over the materials and construction of appliances sold for household use, electrical inspection of all new installations, and prohibition of extending house circuits without permission from the authorities, and the employment of qualified electricians.

Outside of the home, civilians may become exposed to high-tension circuits on the carrying lines of light and power systems. Although all such lines are effectively insulated at their points of support and are ordinarily out of reach of passers-by, trespassers and workmen may come in contact with them while on roofs, in trees, or ladders, etc., and, in the case of third-rail street-car and subway systems, if they happen to short-circuit the third rail. Under exceptional conditions the circuit may be brought to the ground by some object in contact with the open conductor, and produce shock in any one touching that object. A wet tree branch may act in this way and even the stream of water from a hose turned on a high tension wire has produced serious results to the person holding the metal nozzle of the hose. The most serious accidents usually result from hanging, overhead wires.

The prevention of such accidents resolves itself into awareness on the part of the public, and precautionary measures by the responsible authorities. All open high-tension circuits should be conspicuously labeled and warnings posted on the supports of the transmission lines. Trespassing should be forbidden on the rights of way around such towers or cross-country lines and on the entire way of third-rail systems. In each instance the circuit should be protected as far as practicable from contact by trespassers who ignore the warnings.

Regular inspection of all power and light lines must be continuously carried out by responsible owners and controlling authorities. All lines should be free from damage or contact by overhanging branches of trees and wires or other systems which might cross over them. Fire and police authorities should issue adequate instructions for the control of all circuits in the case of emergencies.

A second party may be severely and fatally shocked in attempting to rescue a person who is in contact with an open circuit. Prevention of such secondary shocks is a matter of *knowing the principles* of insulation. The reader is referred to informative sources on first-aid for a more detailed account of what to do in such an emergency. Here it is only necessary to say that the bare hands or any other part of the body are good conductors, and the rescuer must therefore use some poor conductor to pull the shocked person away from the current or the carrier of the current away from the victim.

Whatever is used it should be dry. A pole, stick, branch of a tree, or cane (not an umbrella) can be used either to pry the person loose or push a hanging wire away from the patient. If this cannot be done, the hands may be wrapped with several layers of thick cloth such as a coat, and then the patient or contact maneuvered with the covered hands.

Industrial electrical shocks are preventable by the application on a larger scale and under more controlled conditions of the measures already outlined. In addition, there is the moral and economic necessity for more emphasis on prevention brought about by the Workmen's Compensation Act and Liability Insurance measures.

In the preceding section it was shown that exposure to alpha- and beta-rays of radium occurred among handlers of the radio-active elements, users of luminous paint and the use of radiant waters and radon emanators in actino-hydrotherapy The serious damage produced in those handling radio-active elements for therapeutic and investigative purposes early drew world-wide attention to the need for awareness of the danger and the promulgation of minimal precautionary measures against it. Although individual writers had stressed certain advisable measures, it remained for international cooperative effort to formulate standard recommendations. The latest revision of these recommendations was accomplished by the

International *X*-ray and Radium Protection Commission of Zurich, July, 1934.[1]

The portions of these recommendations which are pertinent to protection against radium are given below:

I. WORKING HOURS, ETC.

(*c*) Not less than four weeks holiday (for radium workers) a year, preferably consecutively.

(*d*) Whole-time workers in hospital *x*-ray and radium departments should not be called upon for other hospital service.

(*e*) *X*-ray workers, and particularly radium workers, should be systematically submitted, both on entry and subsequently at least twice a year, to expert medical, general and blood examinations.

VI. RADIUM PROTECTIVE RECOMMENDATIONS.

(A) Radium Salts.

30. Protection for radium workers is required from the effects of:
  (*a*) Beta-rays upon the hands.
  (*b*) Gamma-rays upon the internal organs, vascular and reproductive systems.

31. In order to protect the hands from beta-rays, reliance should be placed, in the first place, on distance. The radium should be manipulated with long-handled forceps, and should be carried from place to place in long-handled boxes, lined on all sides with at least 1 cm. of lead. All manipulations should be carried out as rapidly as possible.

32. Radium, when not in use, should be stored in a safe as distant as possible from the personnel. It is recommended that the safe should be provided with separate drawers individually protected. The amount of protection should correspond to the values given in the following table; these values, which are based on working conditions where there is proximity to radium, may be reduced for larger working distances.

Maximum quantity of radium element.	Thickness of lead
0 05	5 0
0 2	8 5
0 5	10 0
1 0	11.5
2 0	13 0
5 0	15 0
10 0	17 0

33. A separate room should be provided for the "make-up" of screened tubes and applicators, and should only be occupied during such work.

[1] Reprinted in Radiology, 23, 682, 1934.

(B) Radon.

39. In the manipulation of radon, protection against the beta- and gamma-rays has likewise to be provided, and automatic or remote controls are desirable.

40. The handling of radon should be carried out as far as possible, during its relatively inactive state.

41. Precautions should be taken against excessive gas pressures in radon plants. The escape of radon should be very carefully guarded against, and the room in which it is prepared should be provided with an exhaust fan controlled from the outside of the room.

42. Where radon is likely to come in direct contact with the fingers, thin rubber gloves should be worn to avoid contamination of the hands with active deposit. Otherwise, the protective measures for radium salts should be carried out.

43. The pumping room should preferably be contained in a separate building. The room should be provided with a connecting tube from the special room in which the radium is stored in solution. The radium in solution should be heavily screened to protect people working in adjacent rooms. This is preferably done by placing the radium solution in a lead-lined box, the thickness of lead recommended being according to the table in Paragraph 32.

Except for cases originating from the use of natural or artificial radiant waters chronic radium poisoning is essentially an industrial problem.

The prevention of poisoning from radiant waters may be summed up in the statement that the sale to the public of radon emanators and radium salts for addition to water should be prohibited by law.

In the case of natural radiant spring waters control should be exerted over their use by the medical profession whenever practicable and by constituted health authorities. People using such waters at public or private spas should do so only under competent medical supervision. The public sale of natural radio-active salt waters should be prohibited.

Employees and attendants at spas and radio-active "cure" institutions should be examined frequently for anemia, bone changes and their general physical condition.

When the industrial hazards to luminous paint workers became evident by the appearance of patients with chronic radium poisoning in the watch industry, the United States Public Health Service and cooperating agencies made a thorough survey of the problem. Among the reports issuing from this investigation published under the general title, "Health Aspects of Radium Dial Painting,"[1]

[1] Schwartz, L. *et al.*: Health Aspects of Radium Dial Painting: I. Scope and Findings, Jour Indust Hyg, 15, 362, 1933

were recommendations for the control of this industrial hazard. They are herewith given in full:

Suggestions for Minimizing Hazard of Radium Dial Painting.—With the abolition of the practice of pointing the brush in the mouth, prevention of radium poisoning depends primarily on extreme cleanliness in the factory (*i. e.*, good housekeeping), thorough personal cleanliness of the workers, and adequate ventilation, both general and local. Specific suggestions along these lines follow:

1. Rigid and continuous inspection of all processes involving the use of radium is advisable. *Thus inspectors should be supervised* by a qualified officer responsible directly to the management of the plant.

2. Painting by hand should be done by a method which will eliminate the contamination of the mouth and fingers with radium. The practice noted in several plants was to use glass styluses, or pens.

3. Styluses or pens should be wiped only on cloths (or other suitable material) kept moist with a solvent. One good practice noted was that of using a rubber sponge kept moist with a solvent held in a small container.

4. Racks should be provided so that pens, styluses and stirring rods may be held securely and so that contamination of the workplace with paint from this source may be prevented.

5. Paint containers should not be over ½ inch deep and should be so placed in a holder that retaining them in the hand is unnecessary.

6. Dry paint should be mixed with the liquid ingredient in a hood with openings for the hands only and provided with suitable exhaust ventilation to prevent escape of dust or emanation into the workroom atmosphere. Not more than a day's supply of paint should be mixed at one time, and it should be kept covered in a container lined with lead at least 1 inch thick.

7. In order to avoid any accumulation of radio-active materials in the workroom, it is suggested that mixed paint and materials be given out to the workers in quantities to last for short periods (preferably not longer than one hour), all materials and empty containers to be returned at the end of each period.

8. All materials should be cleaned moist, and discarded materials should be promptly removed from the workroom. The contents of all refuse cans should be removed daily.

9. Moist methods only should be used for removing paint from surfaces and in recovering radio-active materials from old or rejected stock. Cloths used for this purpose should be replaced by fresh ones twice daily. Material collected for radium recovery should be segregated under lead protection and kept in a closed container.

10. Radium material should be stored in containers shielded by

lead and kept as distant as possible from the workers. The lead should be at least 1 inch thick.

11. The room or rooms in which radium painting processes are carried out should be separate from those used for other purposes.

12. The floor and work places should be constructed so that they may be thoroughly and readily cleaned by a moist method. They should be cleaned daily after work hours. Pipes, window sills, and all surfaces upon which dust can accumulate should be cleaned weekly by moist methods.. Wooden floors should be covered with some material which will prevent dust from accumulating in the floor crevices. Work tables or working surfaces should be of some polished, easily cleaned material such as enamel.

13. Ample space should be allowed for each worker.

14. Illumination should be adequate and free from glare, with at least 10 foot-candles on the working plane.

15. Drinking water should be provided by bubbling fountains of the approved slanting jet type. The use of individual drinking cups of any character should not be permitted.

16. Convenient working facilities should be provided with arrangement for mixing hot and cold water in the faucet. At least one faucet should be available for each 5 workers. Paper towels and nail brushes should be provided by the employer.

17. Only neat, careful persons should be employed for radium work.

18. Workers should be provided with clean smocks at regular intervals.

19. Workers should keep their hands and workplaces scrupulously clean at all times, and foremen should see that this rule is rigidly enforced.

20. Eating during working hours and the presence of eating utensils or articles of food in the workroom should be prohibited.

21. The workers should wash their hands thoroughly and clean their finger nails before eating at noon, and after work at the close of the day. This washing should be done under supervision to see that the regulation is properly carried out.

22. Adequate general ventilation should be provided (15 to 20 air changes per hour). Where the concentration of radium dust is high, additional ventilation of a local exhaust type should be installed as recommended or suggested in 6, 23, 24, and 25.

23. Painting by hand should be done beneath a sheet of plate glass, having a plano-convex lens at least 3 inches in diameter cemented to its lower surface. This glass should be large enough to cover all the radio-active material. The lens should be of such a focus that the face of the worker is not less than 14 inches from the work. It is suggested that, if possible, local exhaust ventilation should be provided beneath the glass.

24. Any one who weighs, mixes or distributes radio-active material should be protected from radiation by suitable lead screen and from radio-active dust by ventilated hoods.

25. Inspectors of radium-painted stock should conduct their work at open-front cabinets provided with exhaust ventilation of sufficient quantity to secure an air movement of 100 to 200 linear feet per minute at the face of the cabinet and in a direction toward the back of the cabinet.

26. Because of the high dust concentration, dusting and transfer press work as observed during the investigation should be abandoned or adequately safeguarded.

27. To test the effective enforcement of precautionary measures, periodic examinations, at least annually, including electroscopic tests (gamma-ray and radon), blood examinations, *x*-rays of the maxilla and mandible, and tests of the radio-activity of dust in the workroom air are advised. The results of these examinations should be communicated to the employees.

28. A statement of the precautions to be taken by the worker for the prevention of radium poisoning should be posted in each workroom. All applicants for work should be advised of the hazard and instructed in the observance of necessary precautions.

CHAPTER XXXIX.

CATEGORY V: THE PROCESSES AND EFFECTS OF INVADING ORGANISMS.

LIVING organisms enter the tissues of the human host through their own activity or by passive introduction, and having entered, bring about harmful results through the vital activities of their particular life processes. These organisms are ordinarily called parasites, a term difficult to define because of the connotations generally associated with it, many of which are not essential or even constant. In its broadest sense a parasite is any living organism which subsists at the expense of another. All living organisms which can live on or in the tissues of man and obtain from him some substance which is useful to their own vital processes may be looked upon as human parasites. The intimacy of the relationship, the mutual benefit or harm between the organisms involved and the length of time during which they are associated may therefore be left out of the definition. Such factors only further qualify parasitism and form the basis for the different types and degrees.

Since this work deals with the etiologic factors of disease, consideration will be given only to those parasites of man which are capable of doing harm; *i. e.*, to the pathogenic organisms.

Every organism which has invaded the tissues of man has come from his environment. This is true whether the event occurred prenatally, at the moment of conception, or at any time in the subsequent history of the individual. Etiologically, all parasites are external factors of disease and their existence in the environment antedates any rôle which they may play in the pathogenesis of disease. That they may exist in the human host for many years without producing evidence of harm and then, for some reason, reveal pathogenic qualities, does not lessen the argument that their original source was in the external environment of the host.

The criteria on which parasitic agents are placed in a definite category of causative factors are therefore two in number: (1) They are living agents which produce disease by virtue of the effects of their own life processes; (2) they originate in the external environment and affect man by invading his tissues.

By these criteria the category must include all living pathogenic organisms. A list of them would contain the names of all vegetable and animal organisms which can invade and do harm; it would

include all ecto- and endo-parasites which are pathogenic or potentially so; it would contain all pathogenic parasites of whatever size, whether unicellular or multicellular, microscopic or ultramicroscopic, *filterable or non-filterable*; it would make no distinction between symbionts and non-symbionts, commensals, obligates and facultatives other than as these terms are applied to particular parasites and the qualifications which they express.

It is beyond the scope of this work to enter into a detailed discussion of the genetic relationship between the organisms which are parasitic on man, or to review the evidence pointing toward the phenomenon of adaptation as applied to successful and non-successful parasitism of the human by sub-human organisms. Although some of these aspects must be brought out later, it must suffice to remark at this point that genetic relationships undoubtedly exist between the majority of the biologic groups, and that this relationship has an important bearing on relative pathogenicity. That this is largely a question of adaptation from the evolutionary point of view can hardly be doubted, although the time and circumstances under which this occurred has not yet been disclosed with positive assurance in even a single instance. Nor can pathogenicity and non-pathogenicity be accepted as absolute. Increasing knowledge of variant forms of organisms and possibly also the evidence that different humans show fluctuating and inconstant susceptibility to culturally, morphologically and serologically similar organisms may mean that old forms of parasites may be losing their pathogenicity or non-pathogenic forms are becoming pathogenic, or on the side of the host that factors are at work which are changing the ability of the host to act as a means of supporting life or contributing to the welfare of the parasite.

The point of greatest significance in the concept of parasitism is the fact that the host-parasite relationship is not a struggle in the teleological sense, as is so often implied, but an adaptation, more or less complete, between two organisms which are accidentally brought together in variable degrees of association. This statement will be challenged by those who adhere to purpose as their basic concept and by others who claim that the necessity for certain forms of human parasitism has resulted from a prolonged give and take adaptation between host and parasites which has made their relationship contributory to human survival.

This is of more than academic interest, for much of the effort of medical science is to rid the human of many of its parasites. On the assumption that some parasitism may be useful for individual survival it would therefore become questionable how far science should go in this purifying process. The author is of the opinion that science can hardly go too far in this respect, since to date it has been dealing almost entirely with survival of the individual and

not of the race. There appears to be no evidence that the human race depends for its survival on the support of any parasite.[1]

Pathogenic potential parasites living in man's external environment are found under widely varying conditions and circumstances of their own environment which determine their survival or death, favor their growth and multiplication, limit them as individuals or groups, influence their potentiality for harm in the direction of increased or decreased pathogenicity should they become parasites, and alter their accessibility to and invasibility of the tissues of the human host. They are the products of their environment and subject to it and can do not other than respond in the direction that the environment necessitates. This environment can be deliberately altered by man to the proven disadvantage of the organisms.

Except for a possible few organisms which have become completely parasitized in man, the parasite's existence in the external environment is extremely hazardous. Physical and chemical changes in the environment and the vicissitudes of their association with other living organisms makes survival in their extra-human state a highly doubtful probability unless their lot happens to fall in very favorable circumstances.

Epidemiology is largely concerned with these favorable and unfavorable circumstances, for survival of organisms in their passage from one human host to another is a *sine qua non* of infection and infestation. For this reason Preventive Medicine interests itself largely in the parasitic disease agents as they are in passage from man to man and the chain of circumstances which favor their survival or operate against them.

Although the sciences of bacteriology, parasitology and epidemiology must ultimately concern themselves with the details of the individual pathogens, Preventive Medicine in its broadest scope will deal largely with the basic generalizations that govern the behavior of parasites as a whole. Since the main generalization in prevention is based on the postulate "to oppose or intercept a cause is to prevent or dissipate its effects," it becomes important to review first the loci of parasitic agents in their extra-human existence, then to examine the factors influencing survival, and lastly to investigate the manner in which they gain access to and invade the human host to produce disease. Within the last will be included the mechanisms of defense on the part of the host.

A list is given below of the pathogenic parasites of man. Under each organism will be a short descriptive account of every known

[1] Aside from this argument, the idea that the parasites, especially the bacteria, "attack" us has become obsolete In only few instances where predatory organisms obtain some degree of benefit from the human tissues can the concept of an attack be maintained, but even this must be shorn of its teleologic implications Mosquitoes may appear to attack us to obtain human blood, but they are only hungry for blood and not "bloodthirsty."

locus of the parasite in its entire life history. In several instances a parasite will be found to harbor another human parasite in some stage of its life. This double rôle will necessitate its discussion under two headings, one as a primary parasite and another as a locus of the second parasite. The list has been divided into biologic groups as suggested by Gay[1] and arranged alphabetically within each group.

PATHOGENIC PARASITES OF MAN.

Bacteria.

Bacillus anthracis.—In animals with anthrax; mostly grazing animals. Soil, grasses, dirt and dust. (Pastures may remain infected with spores which have survived for as long as twenty years.) Products of infected animals—hides, fur, hair, wool, blood, and discharges from anthrax lesions of animals and man. Blood-sucking insects.

Bartonella bacilliformis.—*In blood and lesions of oroya fever and verruga peruana.* Possibly in sandfly, *Phlebotomus verrucarum.*

Brucella abortus —In infectious abortion of cattle and hogs. Var. *bovine* (cattle): Organism in vaginal discharge, placenta, fetus, and few in urine, feces and milk. Dairy products—milk, cream, butter, uncooked cow's meat. Man—blood, contaminated hands Var. *porcine* (hog): Organism in vaginal discharge, placenta, fetus, urine and feces. Little known as to its presence in other tissues. Uncooked meat(?) Hog carcasses—flesh, hide. Man—blood, contaminated hands.

Brucella melitensis —Infected goats—blood, milk, urine (even in apparently healthy goats), widespread in tissues. Raw dairy products. Man—blood, contaminated hands.

Clostridium histolyticum.—Soil Possibly in gastro-intestinal canal of man and animals. Gas gangrene lesions in man.

Clostridium novyi.—Soil. Poorly cooked and preserved meats (sausage). Feces of animals. Refuse from manufacture of animal meat products. Gas gangrene lesions in man.

Clostridium œdematis-maligni.—Soil. (Has been demonstrated in virgin soil.) Contaminated vegetables and fruit. Intestinal tract of man and *animals (may possibly adapt itself to intra-intestinal life). Feces.* Malignant edema infections in man.

Clostridium tetani.—Soil. (Especially when cultivated. Has been found in virgin soil.) In intestinal tract of animals and man (especially horses and cattle). Feces. Street dirt and contaminated articles such as boards, wire fences, splinters, nails, rocks and gravel, etc. Contaminated catgut, vaccines, dressings, umbilical ties. Contaminated vegetables and fruit In infected wounds in man. May be present in the mouth around the teeth.

Clostridium welchii.—Soil, water, milk, dust and sewage. Intestinal canal of man and animals. Feces of practically all higher animals. Ubiquitous contaminant of articles of common use.

Corynebacterium diphtheriæ.—In normal bacterial flora of skin and *mucous membranes of many animal species, including man. Human* carriers and latent and active infections in man—nose and throat, skin wounds, vaginal mucous membrane. Droplets in expired air. Questionable persistence on contaminated inanimate objects after the contagium has dried. Virulence of animal types to man questioned.

[1] Gay, F. P. Agents of Disease and Host Resistance, Baltimore, C Thomas, 1935.

Diplococcus pneumoniæ.—Common in normal nasopharyngeal flora of man. Droplets in expired air. Droplet nuclei in room dust.

Eberthella typhi.—Human cases of typhoid fever and carriers—feces, urine, bile, contaminated skin. Contaminated clothing, bed-clothes, dressings and utensils. Water—drinking-water, bath-water, wash-water, wells, cisterns, springs, streams, rivers, lakes and ponds. Soil contaminated with urine and feces of human cases and carriers. Contaminated foods—milk, vegetables (especially uncooked, leafy vegetables and sea-foods). Flies (passive carriers). Food handlers—contaminated fingers of carriers and sick-room attendants.

Escherichia coli.—Typically an intestinal parasite of man and animals. Frequently pathogenic in other tissues. Feces. Urine occasionally. Soil. Contaminated water—drinking, bathing, and washing, household containers, springs, streams, lakes, ponds and rivers. Contaminated skin, clothing, bedclothes, dressings. Hands—physicians, sick-room attendants, uncleanly generally. Flies, cockroaches and other vermin (passive carriers).

Fusiformis fusiformis —Obligated parasite in human mouth. Human cases of Vincent's angina. Teeth and gums.

Hemophilus conjunctivitidis.—Unknown outside of man—human conjunctiva (Koch-Weeks bacillus infection).

Hemophilus ducreyi.—Unknown outside of man—soft chancre.

Hemophilus influenzæ —No evidence of its distribution in nature. (There is no proof of any causal relationship between human influenza epidemics and epizoötics of swine and ferrets) Human—cases of influenza, carriers—in nose and throat. Expiratory droplets and droplet nuclei.

Hemophilus lacunatus.—Unknown outside of man—conjunctiva (Morax-Axenfeld infection).

Hemophilus pertussis.—Human cases of pertussis. (Associated with causative virus.) Expiratory droplets. Contaminated fomites in intimate relationship with cases.

Klebsiella granulomatis.—Unknown outside of man—human cases of granuloma inguinale: in inguinal lesions. (Probably a secondary invader and not the specific causative agent).

Klebsiella ozænæ.—Nose of ozena patients. Nasal mucus and saliva of dogs. (Not established as etiologic agent.)

Klebsiella pneumoniæ (Friedländer).—In normal bacterial flora of respiratory tract of 5 to 25 per cent of people. Expiratory droplets and droplet nuclei. Has been demonstrated in soil, air, dust, mud, and canal water.

Klebsiella rhinoscleromatis —Questionable cause of rhinoscleroma in man. Has been found in man, carp, mice and guinea-pig. Doubtful natural infection in rabbits.

Loefflerella mallei.—Equines—horses, mules, asses (farcy or lumpy jaw)—discharges from suppurative lesions. Demonstrated in cats and dogs. Human—suppurative lesions (glanders). Contaminated dressings, instruments, hands, clothing.

Mycobacterium lepræ.—Known positively only in human—skin, open lesions, nose and throat, feces. Soil—acid-fast organisms not positively identified as viable, pathogenic human leprosy organisms. Contaminated dressings. Bedbugs and cockroaches. Relationship of rat leprosy to human leprosy unknown.

Mycobacterium tuberculosis var. *hominis* —Man—lung lesions, sputum, skin, visceral lesions. Contaminated dressings. Feces, urine. Expiratory droplets in open cases of respiratory system tuberculosis. Contaminated drinking and eating utensils, handkerchiefs, and other intimate fomites. Droplet nuclei—street and house dust, soil. Foods—contaminated milk, especially dairy products. Infected monkeys, dogs, parrots and pigs.

Mycobacterium tuberculosis var. *bovis*.—Infected udder of cows. Milk. Contaminated hands of milkers, cattle handlers, dairy workers. Human lesions. Human feces, urine and infectious discharges. Contaminated dressings, drinking and eating utensils. Natural infection in bovines, pigs, cats, monkeys, horses, rabbits and guinea-pigs. Infected meat foods.

Neisseria gonorrhœæ.—Strict parasite of man. Human lesions—discharges from urethra, vagina, conjunctiva, open surface lesions, semen, urine. Contaminated dressings, clothing, towels, toilet seats, body surfaces (hands), utensils and other intimate fomites.

Neisseria intracellularis.—Strict parasite in nasopharynx of man—cases of epidemic meningitis in man and human carriers. Infected expiratory droplets.

Pasteurella pestis.—Man—plague bubo, blood and sputum. Infected expiratory droplets. Human carriers. Rats (*Rattus rattus, Rattus alexandrinus, Rattus norvegicus*), tarbagan (*Arctomys boboc*), ground squirrel (*Spermophilus seu Citellus beecheyi*), susliks (*Spermophilus rufescens*), cavies, guinea-pig, gerbilles (*Gerbillus taleronia*). Camel and sheep reservoirs questionable. Rat flea (*Xenopsylla cheopis, Ceratophyllus fasciatus*), squirrel flea (*Ceratophyllus acutus*), tarbagan flea (*Ceratophyllus silantievi*), suslik or marmot flea (*Ceratophyllus tesquorum*), gerbille flea (*Dinopsyllus lypusus*), human flea (*Pulex irritans*)? Rodent burrows.

Pasteurella tularensis.—Natural diseases (endemic and epizoötic) of squirrels and rabbits. Has been found in sheep, woodchuck, muskrat, opossum, grouse, water-rat (*Arvicola amphibius*), coyote(?). Rabbit-tick (*Hæmophysalis leporis-palustris*), wood-tick (*Dermacentor andersoni*), dog-tick (*Dermacentor variabilis*), deer-fly (*Chrysops discalis*). Tissues of infected animals—meat, pelt, fur, blood. Man—surface lesions, expiratory droplets. Contaminated dressings, hands of attendants. Laboratory cultures.

Salmonella ærtrycke.—Enteric infection and septicemia in calves, rodents and cattle. Improperly cooked and raw infected meat. Feces of infected animals and man. Blood of animals.

Salmonella enteritidis.—Natural pathogen in cattle and rodents. Feces of infected animals and man. Healthy animal carriers. Feces of animal carriers. Contaminated meat. Meat of infected animals.

Salmonella paratyphi.—Man in enteric fever—feces. Human carriers—feces. Contaminated fingers, food, clothing, drinking water, cooking water.

Salmonella psittacosis.—Parrots. Man (secondary invader).

Salmonella schottmülleri.—Human—cases of food poisoning, carriers—feces. Contaminated fingers, food, drinking and cooking water.

Salmonella suipestifer.—Enteric disease in hog (secondary invader in hog-cholera), feces. Human—enteric fever, feces. Contaminated meats, infected meat.

Salmonella typhi-murium.—Mice—septicemia, feces. Contaminated meats, milk and other food. Human intestine, feces. Contaminated hands. Drinking- and cooking-water.

Shigella dysenteriæ var. *Flexner*.—Human—intestinal tract, feces. Contaminated food, drink, food handlers. Flies (passive carriers).

Shigella dysenteriæ var. *Shiga-Kruse*.—Human—intestinal tract of active cases of dysentery and carriers, feces. Contaminated food handlers. Contaminated food and drinks. Flies. Dog and rabbit infections, feces Contaminated clothing, bedclothing, dressings.

Shigella dysenteriæ var. *Sonne* (Duval).—Human—intestinal tract of active cases of dysentery and carriers; feces. Food handlers. Contaminated food and drink. Flies.

Staphylococcus albus; S. aureus.—Normal flora on skin of man. Human feces Suppurating lesions. Air. Dust. Water. Widely disseminated on common articles. Contaminated clothing, dressings, towels, surgical instruments, etc.

Staphylococcus epidermidis.—Normal flora on skin of man. Human feces. Stitch abscesses. Contaminated dressings and surgical instruments.

Streptococcus epidemicus.—Human—throat in cases of epidemic sore throat; healthy carriers(?). Infected expiratory droplets. Sputum. Contaminated hands Accidental infection of cow's udder. Milk.

Streptococcus erysipelatis.—Human—cases of erysipelas; throat, skin, intestines Contaminated hands, clothing, dressings, towels, instruments and utensils. Infected expiratory droplets(?). *S. erysipelatis* var. *puerperalis* in genital tract. Infected wounds.

Streptococcus hemolyticus var. *pyogenes.*—Natural suppurative and septicemic conditions in animals and man. Infected animal products. Milk. Contaminated skin, hands, dressings, clothing, towels, instruments. Flies and vermin (passive carriers).

Streptococcus scarlatinæ.—Human—skin, throat, sputum of scarlet fever cases, carriers Infected expiratory droplets. Contaminated fomites. Infected udder of cows. Milk.

Streptococcus viridans.—Human—normal flora of mouth, throat and intestines; sputum, feces. Infected expiratory droplets. Dust. Intestinal canal of animals.

Vibrio choleræ (sp).—Human – intestinal canal of cholera patients; carriers. Feces. Contaminated drinking and bathing water, springs, lakes, rivers, pools. Contaminated vegetables and cooking water. Contaminated clothing, bedclothes, dressings, sick-room supplies and utensils. Hands of attendants and food handlers. Flies and cockroaches. Relationship to free-living, saprophytic vibrios in sea water, cheese, river water, intestines of pigs not determined.

Chlamydozoa-Strongyloplasms.

I With cell inclusions. Proven transmissible and filterable.

Foot and Mouth Disease Virus.—Cattle, sheep, hogs, goats, buffaloes, reindeer, camels, guinea-pigs, rabbits. Teats, saliva, tears, nasal discharge of infected animals. Infected milk and dairy products. Contaminated hands. Human disease lesions

Herpes Simplex Virus.—In human lesions. Virus probably ubiquitous but not demonstrated outside man.

Molluscum Contagiosum Virus.—In human lesions Not known elsewhere. Suspected in public baths.

Papilloma of Larynx Virus.—In human lesions. Unknown elsewhere.

Psittacosis Virus.—Parrots, parrakeets, cockatoos, canaries—active diseased birds and carriers, secretions from nose, mouth and procrop; feces; infected expiratory droplets; droplet nuclei from feathers. Human—contaminated hands; lesions in internal organs.

Rabies Virus.—All mammals; dogs, wolf, fox, jackal, hyena, cat, cattle, sheep, goats, horses, swine, bats—saliva, tears, urine of rabid animals. Milk from infected cattle(?) Human lesions

Rift Valley Fever Virus.—Tissues of diseased sheep Hands of contaminated humans.

Vaccinia Virus.—Infected epithelial cells, vesicles, and crusts in pox of cow, calf, buffalo, caribou, camel, goat, horse, sheep, hog, rabbit. Contaminated skin of human contacts. Vaccines. Vaccination lesions.

Variola Virus.—Human smallpox cases—infected expiratory droplets, vesicles, scabs, crusts of skin, nasopharyngeal secretions. Sick-room attendants. Clothes, bedclothes, intimate fomites. Flies and vermin (rarely). Dust.

Verruca Vulgarus Virus.—Human lesions. Udder of infected cow (?).

Yellow Fever Virus.—Human blood. Mosquitoes—*Aëdes ægypti, Aedes scapularis, Aëdes tæniorhynchus* (experimental). Jungle mosquitoes (So. America).

II. Cell inclusions present—transmissible but filterability not proved.

Varicella Virus.—Skin lesions of human chicken-pox cases (vesicle contents). Contaminated skin of human contacts. Intimate fomites, bedclothes, clothing.

Inclusion Blennorrhea Virus.—In lesions in human conjunctiva. Not known elsewhere.

III. Cell inclusions present—not transmissible—filterability not established.

Herpes Zoster Virus.—Questionable demonstration of inclusion bodies in human lesions. Nothing further known.

Filterable Agents Without Cell Inclusions.

Common Cold (Coryza) Virus.—Human nose and throat—nasopharyngeal secretions. Expiratory droplets. Contaminated hands, handkerchiefs, towels and intimate fomites.

Dengue Fever Virus.—Blood of dengue fever cases. Mosquitoes—*Aëdes ægypti, Aëdes albopictus, Culex quinquefasciatus.*

Mumps (Epidemic Parotitis) Virus.—Human cases—saliva, mouth washings. Infected expiratory droplets. Saliva-contaminated hands and articles of general, intimate use.

Pappataci Fever Virus.—Blood of pappataci fever cases. Sandfly or midge (*Phlebotomus pappatassii*).

Poliomyelitis (Epidemic) Virus.—Nasopharyngeal secretions of cases of infantile paralysis; feces(?); blood(?). Carriers. Insects(?)—stable fly (*Stomoxys calcitrans*); house fly. Contaminated food and drink (milk)(?). Expiratory droplets(?); droplet nuclei(?); dust(?).

Diseases Presumably Due to Filterable Viruses.

Epidemic Encephalitis.—*Nasal secretions in human cases(?).*

Epidemic Influenza.—Virus in saliva and throat of man(?). Droplet infection probable.

German Measles (Rötheln).—Nothing known about causative agent.

***Measles* (Rubeola, Morbilli).**—*Probably in nasopharyngeal secretions and* expired droplets.

Multiple Sclerosis.—Nothing known about causative agent.

Rickettsias.

Dermacentroxenus rickettsiæ.—Human blood and tissues in cases of Rocky Mountain spotted fever. Mammalian reservoirs—sheep, horse, dog, cattle, deer, elk, goat, bear, coyote, badger. Tick hosts—eggs, larvæ, adults (*Dermacentor andersoni, Dermacentor variabilis*) transmit rickettsiæ from generation to generation. Larvæ and nymphs in soil, pastures, uncultivated land. Small animal reservoirs—ground squirrel, woodchuck, chipmunk, rabbit, pine squirrel, mice, wood rat.

Rickettsia nipponica.—Kedani mite (*Trombicula akamushi; Trombicula delhiensis*)—larvæ on vole or water-rat, field mouse (*Microtus montebelloi*),

birds(?). Virus transmitted from generation to generation of mite. Water-rat and mouse reservoirs(?). Lesions of human cases of Tsutsugamushi disease (Japanese river fever).

Rickettsia prowazeki.—Blood of typhus patients. Body and feces of body louse (*Pediculus humanus*) fed on blood of epidemic typhus cases. Body and feces of rat fleas fed on blood of endemic typhus cases. Skin of human contaminated by feces and crushed bodies of body lice and rat fleas.

Rickettsia quintana.—Blood, urine, feces and sputum of trench fever patients. Alimentary canal of body louse (*Pediculus humanus*) fed on blood of trench fever cases. Skin of human contaminated by feces and crushed bodies of body lice.

Spirochetes.

Borrelia minus.—Natural disease of rat; in infected mice, guinea-pig, cat, weasel, ferret, squirrel, bandicoot and pig—in tissues of lip and tongue. Blood and local lesions of human cases of rat-bite fever.

Borrelia recurrentis, vars. *duttoni, novyi, carteri, persica.* Blood of human cases of relapsing fever. Ticks (*Ornithodorus moubata* and *Ornithodorus talaje*), East and West Africa—tissues and feces. Bedbug (*Cimex lectularis*), Europe—tissues and feces. Body louse (*Pediculus humanus*), Europe and North Africa—tissues and feces. Tick (Sp.?), United States. Transmitted from generation to generation in the tick. Human skin contaminated by feces and crushed bodies of ticks and lice.

Leptospira hebdomadis.—Field mouse (*Microtus montebelloi*) reservoir—kidney and urine. Blood of human cases of seven-day fever. Human skin contaminated by infected mouse urine.

Leptospira icterohæmorrhagica.—Wild rats and mice—urine. Human cases of Weil's disease—blood and urine. Infected urine-contaminated soil, floors, sewers, trenches, mines, shallow standing water. Human skin contaminated by infected urine.

Treponema pallidum.—Human syphilis cases—tissues, discharges from lesions, semen, blood, fetus and placenta. Contaminated clothes, dressings, drinking and eating utensils, instruments, medical appliances, toilets, intimate personal articles. Contaminated human skin.

Treponema pertenuis.—Human cases of yaws (frambœsia)—discharges from skin and mucous membrane lesions. Contaminated human skin. Fomites, clothing, dressings, bed-clothes Flies (passive vectors).

Treponema vincenti.—Normal flora of human mouth. Abundant in mouth in Vincent's angina and trench mouth. Fomites—drinking and eating utensils, toothbrushes. Possibly only a secondary invader.

Fungi.

Achorion gallinæ.—Human scalp in favus lesions Microsporum of birds.

Achorion schönleinii.—Strictly human in favus of the scalp, skin, nails. Possibly similar to organisms of mouse favus.

Blastomyces dermatitidis.—Human blastomycosis of skin and lung. Similar organism has been found in rotting wood in room Discharges from abscesses Dressings.

Coccidioides immitis.—Human lesions in lungs and skin. Discharges from abscesses, ulcers and sinuses. Organism has been isolated from soil in San Joachim Valley (Calif.).

Cryptococcus hominus (see *Torula histolytica*).

Endodermophyton concentricum.—Strictly human in Tinea imbricata.

Endodermophyton indicum.—Strictly human strain in Tinea imbricata.

Endodermophyton mansoni.—Strictly human strain in Tinea imbricata

Endodermophyton tropicale.—Strictly human strain in Tinea imbricata.
Endomyces capsulatus.—Known only in human lesions—skin, meninges.
Epidermophyton inguinale.—Known only in Tinea cruris, epidermophytosis of foot and eczema marginatum of groin in human. Contaminated clothing and toilet articles.
Hormodendron fontoymonti.—Known only in depigmented skin lesions in man.
Hormodendron olivaceum.—Known only in achromia parasitoria in human skin.
Hormodendron pedrosi.—Known only in chromoblastomycosis in human skin.
Madurella americana (see *M. mycetoma*).
Madurella mycetoma.—Black grains in human mycetoma. Discharge from lesions. Contaminated dressings.
Microsporon audouini.—In lesions of ringworm of the scalp in man. Contaminated toilet articles and clothing.
Microsporon ferruginea.—In lesions of ringworm of the scalp in children.
Microsporon flavescens.—Var. of *M. audouini* in ringworm of the scalp in Brazil.
Microsporon furfur —In human skin lesions of Pityriasis versicolor, Tinea flava. Desquamated epithelium. Contaminated clothing.
Microsporon iris.—Var. of *M. audouini* in ringworm of the scalp in Italy.
Microsporon minutissimum.—Known only in human ringworm lesions.
Microsporon tardum —Var. of *M audouini* in human ringworm of the scalp.
Microsporon umbonatum.—Known only in human ringworm lesions.
Microsporon villosum.—In lesions of ringworm of scalp in Belgium.
Microsporon xanthodes.—Known only in sycosis of the beard in the human. Contaminated toilet articles; razors.
Microsporum fulvum.—Ringworm of human skin. Mice (Argentine).
Microsporum lanosum.—Ringworm of human scalp and hair. Skin and hair of animals, especially dogs. Skin of birds.
Monilia albicans.—Normal flora of skin and gastro-intestinal tract of man. Found in lesions in intertrigo, monilial vaginitis, balanitis, conjunctivitis, meningitis, broncho-pulmonary moniliasis. Variety found normally in gastro-intestinal tract is the causative agent in thrush of the mouth. Contaminated feeding bottles and nipples. Intestinal tract in sprue.
Phialophora verrucosa.—In lesions of skin of feet in human chromoblastomycosis.
Rhinosporidium seeberi.—In human nasal polyp in the tropics.
Scopulariopsis blochi.—Human gummatous lesions of lymphatics resembling sporotrichosis.
Sporotrichum beurmanni (see *S. schenckii*).
Sporotrichum councilmani.—Human case of suppurative arthritis.
Sporotrichum gougeroti (see *S. schenckii*).
Sporotrichum jeanselmei.—Human lesions in gummatous sporotrichosis.
Sporotrichum schenckii var. *S. beurmanni, S. gougeroti.*—Known only in lymphangitic and disseminated lesions of sporotrichosis in man. Horse(?).
Torula histolytica (*Cryptococcus hominis*).—Known only in human lesions in torular meningitis and torula infection of lungs.
Trichophyton acuminatum.—Strictly human endothrix ringworm lesions.
Trichophyton album.—Human ectothrix ringworm. Animal origin probable.
Trichophyton circonvolutum.—Strictly human endothrix infection in the human in the Sudan and Dahomey.

Trichophyton coccineum.—Strictly human ringworm of the skin and nails.
Trichophyton equinum.—Human ectothrix ringworm. Horse.
Trichophyton farinulentum.—Human ectothrix closely allied to *T. mentagrophytes.* Probably of animal origin.
Trichophyton fumatum.—Strictly human ringworm of scalp in Italy.
Trichophyton felineum.—Human ectothrix ringworm. Cat, horse, cattle, sheep, dog, pig.
Trichophyton granulosum.—Human ectothrix ringworm. Horse (Italy).
Trichophyton lacticolor —Human ectothrix ringworm. Probably of animal origin.
Trichophyton mentagrophytes.—Human ectothrix ringworm. Horse, cow, dog, pig, sheep.
Trichophyton megnini.—Human ectothrix ringworm Fowl and pigeon.
Trichophyton ochraceum.—Human ectothrix ringworm. Probably of animal origin.
Trichophyton persicolor.—Human ectothrix ringworm. Probably of animal origin.
Trichophyton plicatile (probably similar to *T. tonsurans*).
Trichophyton radiolatum.—Human ectothrix ringworm. Probably of animal origin.
Trichophyton rotundum.—Human ectothrix ringworm.
Trichophyton rubrum.—Human ringworm of tropics (tinea alba).
Trichophyton soudanensis —Strictly human endothrix ringworm of tinea capitis in Sudan.
Trichophyton sulphurum.—Human endothrix ringworm in England.
Trichophyton tonsurans, vel. crateriformis.—Strictly human endothrix ringworm
Trichophyton violaceum (*T. glabrum*).—Strictly human endothrix ringworm of Italy and North Africa.
Trichosporum giganteum.—Nodular infection of human hair (Piedra).

Actinomyces.

Actinomyces asteroides.—Known only in reported cases of lung lesion and brain abscess in man.
Actinomyces bovis.—In actinomycosis lesions in cattle, swine, horses (rarely in goats, sheep, dogs and cats) In normal human mouth about tartar on the teeth. (There is no evidence of transmission of *A. bovis* from animal to man or man to animal.)
Actinomyces maduræ.—In man in the yellow granules of Madura foot (mycetoma). Saprophytic existence not definitely known.

Protozoa.

Balantidium coli —Non-pathogenic parasite in rectum of pig; vegetative and encysted forms. Cysts in pig feces. Contaminated fingers of swine handlers. Contaminated hog meats, sausages. Intestine of man in balantidiasis—vegetative forms; cysts rarely.
Endameba histolytica.—Vegetative forms and cysts in human intestine in amebic dysentery and carrier state. Cysts in feces; contaminated soil. Cysts in surface drainage water, sewage and contaminated water supplies. Contaminated hands of carriers. Contaminated food and drink, especially raw vegetables and fruits. Rat reservoir? Clothing, bed-clothes and utensils contaminated with cyst-containing feces.
Isospora belli; I. hominis.—Sporozoites in epithelial cells of human intestine in coccidiosis. Oöcyst in feces. Oöcyst containing sporozoites in

contaminated soil. Contaminated vegetables, wash water, drinking water. Contaminated hands.

Leishmania braziliensis.—In lesions of forest yaws (espundia, uta, in South America)—skin ulcers, nasopharyngeal ulcers. Not known outside of human lesions. Experimental infection in sandfly.

Leishmania donovani.—In lesions of reticulo-endothelial system in human kala-azar. *Phlebotomus chinensis* (sandfly). Dog reservoir(?) in Mediterranean regions.

Leishmania tropica.—In surface papule and ulcer of human skin in oriental sore. Discharge from ulcer. Contaminated dressings. Contaminated skin of contacts. *Phlebotomus;* sp.?

Plasmodium falciparum; P. malariæ; P. vivax.—Sporozoites, merozoites, gametocytes in blood of human subtertian (malignant, æstivo-autumnal) malaria subjects. Gametes, zygote, oöcyst, sporozoites in body cavity and salivary glands of mosquitoes (*Anopheles*, sp.).

Sarcocystis lindemanni.—Infected muscles in sheep, pig, rat, mice, cattle. Viable spores in improperly cooked meats. Spores in digestive tract of man before penetrating the walls of the intestine. In the muscles of the heart, larynx and tongue in infected humans.

Trypanosoma cruzi.—Leishmania and trypanosome forms in the tissues and blood of patients with Chagas disease (Brazil, Venezuela, Peru). Intestinal tract of a blood-sucking bug (*Panstrongylus megistus*) fed on infected human blood—rectal cells invaded by crithidia forms; leishmania forms in feces. Human skin contaminated by feces of bug containing leishmania forms. Reservoirs in armadillos, opossums and bats.

Trypanosoma gambiense.—Trypanosomes in blood of human cases of Trypanosomiasis (sleeping sickness). Trypanosomes in proboscis and intestine of tsetse fly (*Glossina palpalis*) fed on infected human blood Developmental and infective forms in salivary glands of tsetse fly. Animal reservoirs, young wild animals of many kinds(?). Nagana (native African domestic cattle) harbor *Trypanosoma brucei*, a similar or adapted form of the human trypanosome.

Trypanosoma rhodesiense —*T. rhodesiense* may be *T brucei* in the human. In intestine of a fly (*Glossina morsitans*) fed on infected human blood. Developmental and infective forms in salivary glands of glossina. Trypanosomes in African domestic cattle (Nagana).

Helminths.

Ancylostoma braziliense.—Filariform larvæ in the skin of human cases of "creeping eruption." Reservoir definitive hosts—dog and cat. Ova in feces. Ova, rhabditiform and filariform larvæ in contaminated soil. Skin of human contaminated with infected soil containing filariform larvæ.

Ancylostoma duodenale; Necator americanus.—Adults in intestinal canal of man in hookworm disease (ancylostomiasis). Ova in feces and contaminated soil. Rhabditiform and filariform larvæ in diluted feces and moist earth. Filariform larvæ on human skin ("ground itch") contaminated by infected dirt. Filariform larvæ in blood-vessels of skin, lungs, trachea, esophagus, stomach and intestine of man

Ascaris lumbricoides.—Adult in intestinal canal of man. Ova in feces (night-soil). Ova on vegetables, drinking water contaminated with infected earth. Ova on contaminated human skin (fingers). (The porcine strain of Ascaris cannot undergo complete development in man nor the human type in the pig.)

Clonorchis sinensis.—Adult flukes in biliary tracts of the definitive hosts—man, cat, dog, hog, skunk, badger, wildcat, marten, mink and guinea-pig.

Eggs in feces. Contaminated water. Eggs in bithyniid snails (*Parafossarulus striatulus; Bithynia fuchsiana; Bithynia longicornis*). Free-swimming cercariæ in fresh water. Cercariæ under scales and in flesh of fresh water Percidæ, Gobiidæ and Anabantidæ. Cyst infected raw fish food.

Dioctophyme renale.—Adult roundworm in kidney of definitive hosts—man, dog, wolf, puma, glutton, raccoon, coati, marten, skunk, mink, otter, seal, ox and horse. Eggs in urine. Intermediate host probably fish (*Idus idus*, experimentally). Infected, raw, fish food(?).

Diphyllobothrium latum.—Adult fish tapeworm in intestinal canal of man who is the definitive host. Eggs in feces. Free-swimming larvæ in fresh water streams, lakes and rivers. Procercoid larvæ in body cavity of small crustaceans (*Cyclops strenuus, C. brevispinosus, C. prasinus, Diaptomus gracilis, D. oregonensis*). Sparganums in body cavity, flesh and connective tissue of fresh water fish fed on crustaceans—pike (*Esox lucius*), perch (*Perca fluviatilis*), Miller's thumb (*Lota vulgaris*), salmon (*Salmo umbla*), trout (*Trutta vulgaris*), lake trout (*Trutta lacustris*), grayling (*Thymallus vulgaris*), rainbow trout (*Onchorhynchus perryi*), barbel (*Barbus vulgaris*), wall-eye (*Stizostedion vitreum*), sand-pike (*Stizostedion canadense griseum*), and burbot (*Lota maculosa*). Infected, raw fish food.

Diphyllobothrium mansoni.—Adult in intestinal canal of man who is its definitive host. Eggs in feces. Intermediate hosts unknown; the first is probably a eucopepod crustacean and the second a vertebrate used as food by man.

Dracunculus medinensis.—Adult guinea-worm in the subcutaneous tissues of man, the definitive host. Ova in pond and well water and other water sources contaminated by eggs extruded through the skin lesion on the definitive host. Larvæ free-swimming in infected water. Larvæ in intestine of minute crustacea (Cyclops) which have ingested them Metamorphosis occurs in *Cyclops quadricornis, C. strenuus, C. viridis, C. bicuspidatus, et al* Drinking and washing water containing infected cyclops.

Echinococcus granulosus.—Adult echinococcus in tissues of definitive host—dog, jackal and cat. Eggs in feces of definitive host. Soil, offal, contaminated with feces containing ova. Ova and developmental stages of larvæ in gastro-intestinal tract and tissues respectively of intermediate hosts—man, sheep (optimal), cattle, pig, horse, camel, goat, monkey, giraffe, tapir, cat, leopard, squirrel and rabbit fed on ova-contaminated food.

Echinostoma ilocanum.—Adult flukes in intestinal tract of definitive host; man. Intermediate hosts unknown; probably two successive species of snails(?).

Enterobius vermicularis.—Man is the only host of the pinworm—adults in intestinal tract; ova on perianal skin and contaminated fingers. Clothing and food contaminated with ova

Fasciola hepatica.—Adult flukes in biliary tract of definitive hosts—man, sheep, ox, goat, buffalo, camel, llama, pig, horse, ass, elephant, wild ruminants, rodents and marine mammals(?). Eggs in feces of definitive host. Miracidium in moist feces and soil water. Intermediate host—snail (*Lymnæa sp.; Ampullaria luteostoma; Isidora tropica; Lymnæa viatrix*), developmental rediæ and cercariæ. Free-swimming cercariæ in meadow water, contaminated water in ditches, pools, streams, flood waters. Cercariæ attached to grasses and water plants (cress). Drinking and cooking water containing cercariæ. Contaminated vegetables. Infected sheep and goat liver used as food.

Fasciolopsis buski.—Adult fluke attached to intestinal wall of definitive hosts—man and pig. Ova in feces (night-soil) of definitive hosts. Free-swimming miracidium in surface waters, pools and contaminated water sources. Infected intermediate hosts—snails (*Planorbis cœnosus; Segmen-*

tina nitidella; Segmentina schmackeri; Segmentina hemisphærula), developmental forms, sporocysts, rediæ, cercariæ in snail tissues. Free-swimming cercariæ in contaminated water sources. Cercariæ attached to aquatic plants; water caltrop (*Trapa natans; T. bicornis*), water chestnut (*Eliocharis tuberosa*), the bulbs and corms of which are used as food by man and pig.

Gastrodiscoides hominis.—Unknown outside of the cecum and colon of the human host.

Heterophyes heterophyes.—Adult fluke in the intestine of definitive hosts—man, cat, dog and fox. Eggs in feces. Stream and river water contaminated by excreta. Intermediate snail host suspected but not demonstrated. Free-living larval stages not known. Encysted larvæ in the flesh of fresh-water mullet (*Mugil cephalis*). Infected fish meat eaten raw.

Hymenolepis nana.—Adult dwarf tapeworm in the intestine of man, rat and mouse. Auto-infectious within the host. Eggs in feces. Fingers and food contaminated by eggs in excreta.

Loa loa.—Adult filaria and microfilaria in tissues and blood of man. Microfilaria in tissues and head structures of the mango fly (*Chrysops dimidiata, C. silacea*) fed on human blood. Human skin infected by microfilaria emerging from the labium of the mango fly.

Necator americanus—Adults of New World hookworm in the intestinal canal of man. Ova in human feces. Ova, rhabditiform, filariform larvæ in night-soil and contaminated earth. Filariform larvæ in contaminated dirt on human skin ("ground itch"). Larvæ in blood, lungs, trachea and gastro-intestinal tract of man.

Onchocerca volvulus.—Adult worm and microfilaria in the subcutaneous tissues of man, the definitive host. Microfilaria in tissues and head structures of the intermediate host, the buffalo gnat (*Simulium damnosum*) and possibly others. On human skin at time of bite by the gnat.

Opisthorchis felineus.—Adult fluke in the intestinal canal of the definitive hosts—man, dog and cat. Eggs in feces of definitive hosts. Water sources contaminated by infected feces. Intermediate hosts not known. Probably a mollusc as the first, and fish as the second intermediate hosts. Infected, raw fish flesh taken as food.

Opisthorchis viverrini.—Adult fluke in intestinal canal of the definitive hosts—man and the civet cat (*Felis viverrus*). Intermediate hosts not determined. Probably present in infected fish meat taken as food.

Paragonimus westermani.—Adult fluke in the lungs of man who is the definitive host. Eggs in the sputum and feces of the definitive host. Sputum or night-soil contaminated surface water, small fresh water ponds, lakes, ditches and streams. Free-living miracidia in contaminated water sources. Developmental stages in first intermediate hosts, melaniid snails (*Melania libertina* (optimum) and probably *M. ebenina, M. hidatchiens, M. multicincta, M. nodiperda, M. obliquegranosa, M. paucicincta, M. tuberculatus*). Free-swimming cercariæ in infected water sources. In soft tissues of second intermediate hosts, fresh water crabs and crayfish (*Astacus japonicus, A. similis, Eliocheir japonicus, E. sinensis, Potamon dehaani, P. obtusipes, Parathelphusa sinensis, Sesarma dehaani, Pseudothelphusia iturbei*). In cooked cyst-infected crab and crayfish meat taken as food. Drinking water containing cysts liberated from infected crabs and crayfish.

Schistosoma hematobium.—Adult worm and eggs in the portal blood and urinary bladder plexuses of man, the definitive host. Eggs in the urine. Eggs and free-swimming miracidia in urine-contaminated surface water in shallow pools, drains, ditches, canals, streams, sewage, public baths and wash-pools. Miracidia and cercariæ in infected tissues of snails (*Bullinus (Isidora) dybowski, B. contortus, Physopsis africana, Planorbis metidjensis*

var. *dufouri*). Free-swimming cercariæ in infected water sources. On human skin wet with water containing infective cercariæ.

Schistosoma japonicum.—Adults and ova in the walls of the intestine and ova in the intestinal canal of man, domestic mammals, and field mice, which are the definitive hosts. Eggs in feces and night-soil. Eggs and miracidia in water of shallow lakes, ponds, streams, canals, irrigation ditches, bathing and washing places and rice-field water (the miracidia are found mostly near the surface of the water). Miracidia, sporocysts and cercariæ in soft tissues of molluscan intermediate hosts (*Katayama nosophora, Oncomelania hupensis, Katayama formosana*). Free cercariæ under the surface film of still water sources as above. Infected water and water film on the skin of mammals.

Schistosoma mansoni.—Adult in mesenteric veins of the intestinal wall in man, the definitive host. Eggs in the feces of the mammalian host. Eggs and free-swimming miracidia in diluted night-soil and contaminated surface water, pools, streams, ditches, canals, sewage, lakes and irrigation ditches. Miracidia, sporocysts and cercariæ in soft tissues of the intermediate molluscan host (*Planorbis boissyi, P. pfeifferi, Physopsis africana, Planorbis sudanicus, P. olivaceus, P. centrimetralis, P. guadeloupensis*). Free-living cercariæ in contaminated water. Infective cercariæ on the human skin wet by contaminated water.

Strongyloides stercoralis.—Adult female of the parasitic generation in the intestinal wall of man, eggs in the epithelial glands and lumen of the intestine; rhabditiform larvæ in the intestinal lumen. Rhabditiform and filariform larvæ in the night-soil and feces-contaminated earth (heterogenetic cycle in dirt). Hands, vegetables and other foods contaminated with dirt containing infective filariform larvæ (Oral mucosa and skin may be directly contaminated.)

Tænia saginata.—Adult beef tapeworm in intestinal canal of man, the definitive host. Ova in feces of definitive host Ova in contaminated earth, pasture land, grasses Larvæ (bladderworm, *Cysticercus bovis*) in the pterygoid muscles, tenderloin and heart of the ox (intermediate host) which has fed on infected food. Other intermediate hosts are the buffalo, giraffe and llama. Viable cysticerci in infected meat from the intermediate host.

Tænia solium.—Adult pork tapeworm in the intestinal canal of man, the definitive host. Ova in feces of definitive host Ova in feces-contaminated earth, grass, offal and surface water. Larvæ in the muscles of the intermediate host—pig, sheep and dog as *Cysticercus cellulosæ* Infected raw or poorly cooked pork products ("measly" pork).

Trichinella spiralis.—Adult male and female worms in or on the intestinal wall of the definitive host; viviparous larvæ in mesenteric vessels, general circulation and striated muscles of hosts—man, pig, rat (black and brown), wild boar, dog, cat, fox, bear, marten. The rat and pig are probably the common reservoir hosts. Viable larvæ in the animal food of the cannibalistic rodent reservoir hosts and the flesh-eating mammalian hosts. Viable larvæ in pork improperly cooked as food for man.

Trichocephalus trichiuris—The adult whip worm is found only in the intestinal canal of man. (Pig?) Eggs in human feces and night-soil. Embryonated eggs in earth. Vegetables and fruits contaminated with dirt containing viable eggs. Eggs in stomach and intestinal canal of man.

Wuchereria bancrofti—Adult filaria in lymph glands and lymph channels and microfilaria in superficial blood of man, the definitive host. Microfilaria in stomach and head parts of the intermediate mosquito hosts (*Culex fatigans* (most common), *C. pipiens, Aëdes ægypti, A. variegatus, A. togoi, Mansonia pseudotitillans, M. uniformis, Anopheles albimanus, A. rossi, A. costalis, A. algeriensis, A. nigerrimus*). Microfilaria on the human skin at the site of the mosquito bite.

Arthropods.

Aëdes ægypti, and other species of *Aëdes*. The adults of these mosquitoes are common house-frequenting types. Only females bite and are seldom found more than a few hundred yards from their breeding place. *Aëdes ægypti* breeds by preference in still-water containers—cans, tubs, buckets, flower pots, bottles, tree holes, cocoanut shells, etc. Other less important species breed in rot-holes in trees, banana stumps (*A. luteocephala*), rock pools, and cement drains (*A. vittata*). Eggs, larvæ and pupæ in breeding places. Parasitic on man only to the extent of requiring a blood meal. *Aëdes sollicats* breeds in salt marshes and may travel 40 miles on offshore winds.

Anopheles, sp.—Domestic and sylvan mosquitoes. The eggs are laid only in natural waters supplied with water plants—stream banks, bayous, clear lakes, ponds, ditches, fresh water marshes, borrow pits, gutters, wells, cisterns, springs, hollows in bamboo, palms and fiber plants. Larvæ and pupæ develop in the same localities. Adults may travel a few miles but are not carried by high winds. Common inhabitants of houses, buildings, ships, trains and other closed vehicles. Parasitic on man only to the extent of requiring a blood meal.

Anthomyia canicularis.—Garbage fly. Developmental stages in garbage and refuse. Adult frequenter of human habitations. Larvæ on vegetables. Larvæ in intestinal canal of man (accidental intestinal myiasis).

Anthomyia pluvialis.—Garbage fly. Habits similar to *A. canicularis*. Larvæ in skin and body cavities of man. (Accidental cutaneous and tissue myiasis.)

Aphiochæta, sp.—Adults around decomposing matter of all kinds. Oviposit on meats, excreta, vegetable and organic matter, human food. Larvæ in intestinal canal of man (accidental intestinal myiasis).

Calliphora erythrocephala, C. vomitoria.—Adult blow-fly found around decaying animal matter on which it oviposits. Prepupal stage buried in the ground in neighborhood of its hatching place Eggs deposited rarely in human tissues. Larvæ in human intestinal canal (accidental intestinal myiasis). Larvæ in discharges from open sores and wounds on animals and man (semi-specific myiasis).

Chrysomyia bezzianum.—Adult blue-bottle fly which is a specific myiasis-producing fly in man and animals. This fly is rarely seen on foodstuffs as are other species of harmless saprophytic species of *Chrysomyia* Larvæ in intestinal canal of man and animals.

Chrysomia macellaris (var *americana*).—Blue-bottle fly. The adult oviposits in all forms of dead organic matter, in garbage and offal and the tissues and discharges from lesions in animals and man. Larvæ develop at site of oviposition in the ground. Larvæ in tissue myiasis in man (nose, ear and vagina). Tissue larvæ known as the "screw-worm."

Cimex lectularius; C. hemiptera.—*C. lectularius* is the adult temperate bedbug. Eggs in cracks and crevices of rooms, buildings, furniture. Larvæ, nymphs and adults in same localities. Adults may travel the width of a room for a blood meal. Parasitic on man only to the extent of requiring a blood meal. The tropical bedbug, *C. hemiptera*, differs in its habits from the temperate variety only in that it frequents out-houses and animal pens as well as human habitations.

Compsomyia viridula.—Larvæ of fly in the materials of open suppurating wounds. Nose in nasal myiasis (accidental myiasis).

Cordylobia anthropophaga; C. rodhaini.—Larvæ of the fly "ver du Cayor," or thumber fly, burrow into the skin (specific myiasis). Eggs laid on clothing(?); ground(?); floor. Eggs and larvæ in dirt and feces on the floor

of dwellings from which larvæ wander to human skin. Myiasis also occurs in monkey, goat, cat and dog.

Culex, sp.—A house-breeding mosquito but also found distant from human habitation. It oviposits and breeds essentially in relatively dirty water such as is found in gutters and ditches, stagnant pools, overflows from sewage disposal systems, septic tanks, stagnant water in tree-holes and collected in receptacles of many kinds. Parasitic on man only to the extent of requiring a blood meal.

Cynomyia mortuorum.—The larvæ of this sarcophagous blow-fly has been reported in surface ulcers and in the intestinal tract of humans (accidental myiasis).

Demodex folliculorum.—Known only in sebaceous glands and hair follicles (blackheads) in man. It is questionable that they are the active agents of any skin disease in man.

Dermacentor andersoni.—The adult wood tick is an ectoparasite of man, sheep, cattle, goat, horse, deer, elk, bear, coyote and badger. Engorged females and seed ticks (first generation larvæ) in undergrowth, grasses and natural shelters on the ground. Seed larvæ as ectoparasites on ground squirrel, chipmunk, woodchuck, weasel, rabbit, pine squirrel, field mouse and wood rat. Nymphs in ground over winter and in spring on small rodents. (The carrier of *Dermacentroxenus rickettsiæ; Pasteurella tularensis.*)

Dermacentor variabilis.—The adult dog tick and an occasional ectoparasite of man. Female and larvæ in ground. Nymphs on dog. Adult on dog and man. (Carrier of *Dermacentroxenus rickettsiæ; Pasteurella tularensis.*)

Dermatobia hominis.—Adult fly deposits eggs on abdomen of small flies, insects, ticks and mosquitoes. Larvæ leave eggs in contact with warm skin of mammalian host. Larvæ in skin of human and as warbles in cattle, pigs, dogs and other domestic animals Larvæ drop to soil and metamorphose.

Eristalis tenax.—Adult is a large, bee-like hover or drone fly. Commonly found around drains and ditches. Eggs deposited as a heaped-up mass on stones, twigs, etc., at the margin of stagnant water containing decayed animal and vegetable matter, barnyards, manure heaps, etc. Water and food contaminated with *Eristalis* larvæ Larvæ in the intestinal canal of man (accidental myiasis).

Fannia canicularis, F. scalaris, and others.—Small, dark colored adult flies frequenting dwellings and stables. Eggs deposited on decayed fruit, garbage, offal, skin of man, or dirty clothing and napkins Larvæ in intestinal canal, urinary bladder, anus and ear of man (accidental myiasis)

Gasterophilus, sp.—Large hairy flies Eggs deposited on the long hairs on the forelegs, hind legs and abdomen (*G. intestinalis*); lower jaw (*G. nasalis*) and lower lip (*G. hæmorrhoidalis*) of the horse Larvæ in skin and duodenum of the horse. Larvæ in the gastro-intestinal tract of man (specific myiasis).

Glossina palpalis.—Tsetse fly. Inhabits forest undergrowth near water. Larval stages in uterus of female (viviparous). Parasite of man and large mammals only insofar as it requires a blood meal

Glossina morsitans.—Tsetse fly inhabiting open, short-grassed jungle clearings, not particularly near water but near available mammalian hosts Parasite on man and large mammals only for blood meal

Glycyphagus domesticus.—Adult mite in hay and vegetable matter, foodstuffs. Adult skin only during act of biting ("grocer's itch").

Helophilus pendulus.—Small fly frequenting garbage heaps and stable yards Eggs and larvæ in rubbish heaps, manure, rotting fruit. Larvæ in drinking water and fruit. Larvæ in human intestine (accidental myiasis).

Hippelates pusio; H. flavipes.—A small eye-fly, common in public rooms, schools and other indoor meeting places. Adults in conjunctival sac of man.

Hypoderma bovis; H. lineatum.—Adult cattle-warble fly. Eggs on stiff hairs of legs and underparts of cattle. Larvæ beneath the skin and in internal organs (during wandering) of cattle. Eggs on human clothing. Larvæ in human skin and internal organs (accidental cutaneous myiasis).

Leptus autumnalis.—The adult is a variety of harvest mite inhabiting moist ground covered with low vegetation such as berry patches, weed, grain fields, grass and shrubbery. Eggs laid in the ground. Larvæ attach themselves to passing animals such as rabbits, small wild animals, birds, amphibia, dog, cat, cow, horse and man (gooseberry-mite, bête rouge, red bug, chigger, and other local names). Engorged larvæ and metamorphosing larvæ in the ground to which they have fallen from their temporary hosts.

Lucilia sericata; L. cæsar, L. nobilis.—Adult; large metallic "sheep-maggot" flies. Eggs deposited on sheep wool, and in the open sores of humans. Larvæ in ulcers and wounds of sheep and man and in aural cavities and intestinal tract of man. (Semi-specific myiasis.)

Musca domestica.—The common house-fly. Ubiquitous about all human habitations. Eggs deposited in animal manure, human feces, feces-contaminated clothing, decayed and rotting vegetable and animal matter (carcasses). Larvæ in material in which they hatched and third stage larvæ in the ground. Larvæ in wounds, aural cavities and intestinal tract of man. (Semi-specific myiasis.)

Œstrus ovis.—The nasal bot-fly of sheep. Eggs deposited around nostrils of sheep and antelope. Larvæ in nose, accessory sinuses, ear and eye of sheep. Larvæ in ground after dropping from sheep. Eggs deposited by adult fly around the human eye. (Ophthalmomyiasis, specific myiasis.) Habits of adult fly little known except that it hovers around sheep.

Ornithodorus moubata.—Adult tick responsible for transmission of *Borrelia recurrentis* var. *duttoni.* Eggs deposited in cracks and crevices of floors and walls of rest-houses and native huts. Larvæ, nymphs and adults in same locations. Nymphs and adults attached to human skin in act of feeding. Parasitic on man only insofar as it requires a blood meal.

Ornithodorus talaje.—Adult tic, responsible for transmission of relapsing fever in Panama, Mexico and Texas. Eggs deposited in crannies of native beds where metamorphosis of nymph stage occurs. Adults and nymphs in same location. Nymphs and adults attached to human skin in act of feeding. Parasite of man only insofar as it requires a blood meal.

Pediculoides ventricosis.—Eggs of adult grain-itch mite deposited on stalk of cereal grains (corn and barley). Adults hatch directly from egg and feed on vegetable juices and insect hosts (grain moth, peach twig borer, bean and pea weevils, wheat joint worm, cotton boll worms) and the larvæ of hymenoptera and coleoptera. Adults on human skin of cotton-handlers, grain workers, dock laborers, and anyone in contact with infested straw. In mattresses.

Pediculus humans var. capitis.—Adult human head-louse. Eggs laid on human hair. Larval and nymph stages on human hair. Adults among human hairs, especially on the scalp, but may spread to other hairy regions. Adults on hats, caps, capes and other headgear.

Pediculus humanus var. corporis (vestimenti).—Adult human body-louse (clothes louse). Eggs laid on body coverings, especially woolen fabrics in seams and folds. May be laid also on human skin under filthy living conditions and habits. Larvæ and nymph states in clothing. Larvæ, nymphs and adults attached to human skin in act of feeding. Adults travel quickly along clothing and are found more densely on outer garments than those directly in contact with the skin.

Phthirius inguinalis (*pubis*).—Adult crab-louse or pubic louse deposits eggs on the hairs of the pubic and perianal regions and to a far less frequent extent on the eyebrows, beard, moustache and eyelashes. Larval and nymph stages in same regions. Larvæ and adults attached to human skin in act of feeding. Adults may be found in clothing.

Porocephalus armillatus.—Adult tongue worms in liver and lungs of python, adder and viper. Eggs in feces of snake hosts. Eggs in water. Nymph in liver of man, monkey, dog, lion, tiger, wolf, hedgehog, rat and antelopes.

Pulex irritans.—Adult human ectoparasitic flea, found also on rats and other domestic animals. Eggs deposited among hairs of animal host and fall to the ground. Eggs, larvæ and pupæ found in cracks of floors, carpets and among refuse. Adults on human body and parasitic insofar as they obtain blood meals through the skin.

Rhizoglyphus parasiticus—An adult itch mite of man. Adults, larvæ and nymphs among vegetation, especially old tea gardens. All stages of mite in human lesions of skin ("water-itch," "coolie-itch").

Sarcophaga carnaria, S. hæmorrhoidalis; S. lambens.—Adult is the common flesh-fly. Larvæ deposited (viviparous) in vegetable and organic matter and excrement. Larvæ in contaminated food. Larvæ in gastro-intestinal tract of man. Larvæ deposited in open sores and ulcers (especially syphilitic) of man (cutaneous and nasal myiasis).

Sarcophila latifrons, S. ruralis.—Larvæ of this blow-fly found in open ulcers on the human.

Trombicula akamushi.—Adult red mite, kedani or hairy mite of Japan on its common rodent host, the field mouse (*Microtus montebelloi*), other rodents, birds, domestic fowl, pheasants, quail, dog, cat, horse, buffalo and man. Adult in ground along stream margins undergoes metamorphosis. Nymph on potatoes, melons and other vegetables. Pupæ in the ground. Adult oviposits in earth.

Trombicula schüffneri.—A red mite common in jungle adjacent to tobacco fields. Adult hosts, small rodents and birds. On skin of man.

Trombicula deliensis.—A red mite common on palm oil estates. Common host is the rat. On skin of man.

Other *Trombiculæ* found throughout the world as parasites on rats, rodents, fowl and other birds. Known by various local names as they attack man and produce a dermatitis

Tyroglyphus longior; var. castellani; var. siro—The adult mite lives in copra dust (var. *castellani*), farinaceous foods and vanilla (var. *siro*). On human skin ("copra itch," "vanillisme") during the act of biting. In human intestine (accidental parasitism).

Wohlfahrtia magnifica, W. vigil—Adult, sarcophagous "flesh-fly." Eggs deposited in decaying flesh and in the open sores of animals and man. Larvæ in the ground under decaying animal matter. Larvæ in ulcers of the eye, ear, and nose of animals and man and in the healthy skin of man (*W. vigil*). (Semi-specific myiasis.)

CHAPTER XL.

FACTORS AFFECTING SURVIVAL OF HUMAN PARASITES.

SINCE all of the organisms under consideration are parasitic on man, the human host must be a factor in their ecology. His importance to their survival will be in proportion to their dependence on what man has to offer in the dual relationship. This importance will be a measurable function of all other ecologic factors. For example, when man is an obligate host for an obligate parasite this relationship supersedes all physical and chemical factors in the environment insofar as successful survival of the parasite race is concerned, while if man is an alternate host for a parasite which can survive as long as it can find another alternate host, man is relatively of less value.

Under other conditions the parasite-human host relationship becomes of little significance in comparison to the environmental factors which determine the intensity of the parasite's extra-human struggle for existence. The human host can be of little concern if the parasite cannot outlive the other manifold hazards of its life. The measure of these values has not yet been obtained, but there is no reason to question that mathematics may not some day permit a quantitative interpretation of the factors now being examined in experimental epidemiology.

There are many organisms that are strictly human parasites, and so far as is known cannot exist except in continued intimate relationship with man. So long as these parasites retain their ability to invade his tissues and man does not succumb too readily to their activity or overwhelm them, the human host will remain as the greatest asset to their survival. It is difficult to know in many instances how strictly necessary man is to some parasites, for just because no extra-human existence has been determined for them it does not prove that they may not live elsewhere in some so-far unrecognized form or unsuspected locus. This is probably so in the case of some of the fungi, and must certainly be so in at least a few of the ultramicroscopic viruses that have been demonstrated only in man. But, these probabilities aside, the availability of a susceptible human host, is a *sine qua non* of continued existence.

PARASITES DEPENDENT SOLELY ON MAN.

When man is the sole host, the survival of the parasite species must ultimately depend on the transferral of the parasites to another human host. The list given herein contains those organisms which

are believed to be transmitted almost without interruption and without known mediation from man to man. The length of time in transit is so evanescent as to permit little opportunity for extra-human factors to affect them. If they possess mechanisms permitting longer than a few hours independent existence they will not be included in the list.

Fusiformis fusiformis
Hemophilus conjunctivitidis
Hemophilus ducreyi
Hemophilus influenzæ (swine and ferret?)
Hemophilus lacunatus
Klebsiella granulomatis(?)
Mycobacterium lepræ(?)
Neisseria intracellularis
Herpes simplex virus
Molluscum contagiosum virus
Papilloma of larynx virus
Herpes zoster virus
Poliomyelitis virus(?)
Epidemic encephalitis virus (?)
Epidemic influenza virus(?)
German measles virus
Achorion schönleinii
Endodermophyton concentricum
Endodermophyton indicum
Endodermophyton mansoni
Endodermophyton tropicale
Trichophyton fumatum
Trichophyton rotundum
Trichophyton rubrum
Trichophyton soudanensis
Trichophyton sulphurum
Trichophyton tonsurans
Trichophyton violaceum
Endomyces capsulatus
Hormodendron fontoynonti
Hormondendron olivaceum
Hormondendron pedrosi
Microsporon ferruginea(?)
Microsporon flavescens(?)
Microsporon iris(?)
Microsporon minutissimum(?)
Microsporon tardum(?)
Microsporon umbonatum(?)
Microsporon villosum(?)
Microsporon xanthodes(?)
Phialophora verrucosa
Rhinosporidium seeberi
Scopulariopsis blochi
Sporotrichum councilmani
Sporotrichum jeanselmi
Sporotrichum schencki
Torula histolytica
Trichophyton acuminatum
Trichophyton circonvolutum
Trichophyton coccineum
Trichosporum giganteum
Actinomyces bovis
Actinomyces asteroides
Leishmania braziliensis
Gastrodiscoides hominis(?)
Demodex folliculorum(?)

More will be said later of the human factors involved in resistance to invasion and immunity, but the variability of these factors is one of the influences which favors the survival of invading parasites. Any lowering of the threshold which will ordinarily restrain parasites from entering the body may favor their survival. The qualification is made because the threshold to invasion may be low, but the other defense mechanisms may be lower, the host may perish quickly and carry the parasites with it to their doom. If, however, the host is able to overcome the invasion in part and thus survive the onslaught, a long latent infection may result which will be highly advantageous to the invading organism.

Virulence of the organism is also variable in many instances and this may operate in a similar way to enhance the parasite in gaining a successful foothold in its host. All other factors being equal, an organism of low virulence but one which is strong enough to pass the major defenses of the host may set up a sub-lethal infection which persists for months or even years.

Other factors of importance in the host of the strictly human, as well as the obligate human parasites, are the local conditions which exist in the anatomic parts for which the organisms have a special predilection. Most of the clostridia are favored by anærobic environments and the presence of devitalized tissues; fungi by the degree of moisture and heat; some respiratory invaders, by preëxisting infective agents; some intestinal parasites by favorable diets of the host; ectoparasites, by protective clothing, hairiness, exudates, damaged tissues and abnormal secretions; many organisms which constitute the normal fauna and flora of the body, by concurrent changes in physical and physiologic states of the parts which permit these otherwise harmless parasites to exhibit their potential pathogenic qualities.

The entire success of parasites brought into relationship with the host may depend on the characteristics and accessibility of the atria by which they gain entrance to the body. Organisms of the typhoid-dysentery groups are almost entirely unable to produce disease unless they come by way of the alimentary tract. *Corynebacterium diphtheriæ* may invade not only by way of the upper respiratory system but is also able to implant itself successfully on *other mucous membranes opening externally, and even the skin* under favorable circumstances. Most of the pyogenic organisms possess a potentiality for entering by way of the skin and all normal and abnormal orifices. The majority of these successes are due primarily to adaptive properties which are dependent on genetic factors, but others such as the myiases produced by some fly larvæ are accidental adaptations to the human host, because the materials in which they survive are non-living and similar in their important qualities to the parasites' more common habitats outside of man.

The accessibility of the atria will be dealt with further in the discussion of the factors which favor the approach of the parasites to the human body.

The ecologic factors which operate outside of the human host exert their influences so variably on the different forms of parasites that there can be little advantage in taking them up categorically. Instead, the classification of organisms already adopted in this section, affords the opportunity of reviewing the parasites *in seriatum* and recording the effects of environmental factors common to all groups.

BACTERIA, VIRUSES, RICKETTSIÆ AND SPIROCHETES.

There are certain innate faculties in bacteria which are survival assets. Because it is postulated that they are pathogenic to man, it must follow that any mechanisms which they possess for invasion and pathogenesis will be of advantage to them so long as their

properties are reflections of adaptation. In general, this is true of all pathogenic bacteria, although occasions may arise when these properties destroy the supporting host. The higher the mortality rate in man and the more quickly fatal the disease, the less advantage this is to the parasite.

Genetic variations or mutations and changes in the types of physiologic activity of bacteria under certain environmental conditions have been repeatedly demonstrated in the laboratory. These have been correlated in different ways with virulence and invasiveness. The question arises whether these changes in the parasite can account for the apparent changes in virulence under natural conditions. Webster and Flexner in America, and Topley, Greenwood and Wilson in England, have carried on extensive tests on animal populations in an attempt to determine the true nature of this "apparently" enhanced virulence. The sum of this work to date is well expressed in the writings of two authoritative observers and investigators in their own right:

Gay[1] says, "The discovery of Webster and his colleagues, that microbic virulence is apparently a relatively stable property when examined under natural and controlled conditions, has come as a surprise to some pragmatic immunologists who have sponsored the idea that the coming and going of epidemic disease is essentially due to corresponding changes in virulence of the incitant. It is too early to say whether the outcome of these experiments would justify the general deduction that fluctuations in virulence are of no significance in the epidemicity of all diseases. The available data on the virulence of carrier organisms in human infections present *a priori* both conflicting and corroborative evidence. It is also true that the teachings of immunology in the past have relied too largely on conclusions derived from laboratory observations which hold only under a given set of conditions. While it is a generally accepted fact, for instance, that virulence may be increased by rapid animal passage, when such experiments are carried out with animals naturally susceptible to the contagion, and the infectious agent is introduced through a natural portal of entry (respiratory or intestinal tract, as the case may be) there is little or no evidence that enhancement of virulence occurs. Occasionally the opposite may even be *true*. It is possible, of course, that biologic properties of the parasite other than virulence as here defined assume a share in the evolution and involution of epidemics, but since we have no means for measuring such characters, this statement remains, as yet, purely hypothetical." Dudley[2] concludes, "While the direct mutation of one kind of pathogenic parasite into another may not often

[1] Gay, F. P.: Agents of Disease and Host Resistance, Springfield, Ill., Charles C Thomas Company, 1935

[2] Quoted from Dudley, S. F.: Proc Roy. Soc Med., 30, 57, (Sect. Epidem., p. 1) by permission of the Honorary Editors.

be responsible for epidemic phenomena, yet mutations must frequently happen among the pathogenic protozoa, bacteria or viruses, as in all other living organisms. The vast majority of such mutations, having no survival value, die out at once, swamped by the normal offspring of the parent strain. Only on rare occasions will a mutation chance to arise when the conditions give it survival value over the other variants of the same species. But at such moments the new variant could spread and gradually replace, temporarily or permanently, any other variants of the species which were less closely adapted to the environmental conditions of the moment, and it is becoming more and more evident that 'new' diseases, epidemics and changes in the clinical characters of endemic and epidemic illnesses are sometimes as much the result of parasitic variation as of changes in host-resistance and environment."

Most of the pathogenic *Bacilli* and *Clostridia* possess the power of spore-formation. Although the function of spores may not be explainable entirely on the supposition that they are defense stages of the organism against adverse environmental influences they undoubtedly serve in this capacity at least in part. Insofar as they do this they endow the organism with a mechanism of distinct survival value. *Cocci* which do not form spores are relatively much more defenseless against changes in temperature and moisture than the spore-bearers.

The present state of knowledge in respect to bacterial life-cycles does not permit any valid generalizations to be made on the value of the different stages of such a cycle to the adaptation and survival of the organism. Zinsser is of the opinion that spores may be some evidence of a life-cycle in spore-bearing organisms, and that there are other forms in which some bacteria may appear which are filterable. Hadley and others have described bacterial "fragments" called gonidia which he believes are involved in bacterial cyclogeny. The G-type, minute filterable forms of Hadley, Mellon's filterable tubercle forms, Kendall's filterable cocci and typhoid bacilli and Kahn's *segmentation granules of the tubercle bacillus have all been* put forward as cyclogenic phase organisms. Reference has been made to them here only because the possibility still exists that the empiric observations so far made may conform later to further generalizations on bacterial cyclogeny, and possibly bear some more definite relation to survival, virulence and pathogenicity.

The phenomenon of dissociation in bacteria is, without question, correlated with infectivity in some way. It is beyond the scope of this work to go into the structural and functional changes which in turn seem to be correlated with these culture types of organisms and the reader is referred to the current literature on this all-important subject. The correlation with virulence, whether direct

or indirect which these phenomena show will certainly have a bearing on survival.

Many bacteria and viruses are as much, or more, dependent on animal hosts other than man than upon man himself. As in the case of man there is a gradation in the importance of these animal hosts to their parasites which is in proportion to the absolute or relative dependence of the parasites on them for survival. These animal hosts range from the lowest forms of arthropods to the primates. Because these reservoirs are important loci of the parasites in man's environment and therefore point out situations in which they may be deliberately attacked in an attempt to control disease, it will be useful to list the human parasites according to the animal hosts in phylogenetic order. No consideration will be given to whether the hosts are definitive or intermediate, temporary or accidental, because destruction of the host, or the parasite in the host, or disturbance of the host-parasite relationship in any way will be effective in preventing or limiting the survival of the parasite at this location.

Animal Hosts (Natural) of Bacteria, Viruses, Rickettsiæ and Spirochetes.

Monkey: *Mycobacterium tuberculosis hominis, M. tuberculosis bovis.*
Cat: *Loefflerella mallei, Mycobacterium tuberculosis bovis;* rabies virus.
Fox: Rabies virus.
Wolf: Rabies virus
Coyote: *Dermacentroxenus rickettsiæ.*
Jackal: Rabies virus.
Hyena: Rabies virus.
Dog: *Klebsiella ozenæ(?), Loefflerella mallei, Mycobacterium tuberculosis hominis,* rabies virus, *Dermacentroxenus rickettsiæ.*
Weasel: *Borrelia minus*
Badger. *Dermacentroxenus rickettsiæ*
Woodchuck: *Pasteurella tularensis, Dermacentroxenus rickettsiæ.*
Ferret: *Hemophilus influenzæ(?), Borrelia minus.*
Bear: *Dermacentroxenus rickettsiæ.*
Camel: *Pasteurella pestis(?),* foot and mouth disease virus, vaccine virus.
Cattle: *Bacillus anthracis, Brucella abortus, Clostridium tetani, Clostridium welchii, Escherichia coli, Mycobacterium tuberculosis bovis, Salmonella ærtrycke, Clostridium histolyticum, Salmonella enteritidis, Staphylococcus*[1] *sp., Streptococcus epidemicus, Streptococcus scarlatinæ, Clostridium novyi, Clostridium œdematis-maligni,* foot and mouth disease virus, rabies virus, vaccinia virus, verruca vulgaris virus(?), *Dermacentroxenus rickettsiæ.*
Buffalo: Foot and mouth disease virus, vaccine virus
Goat: *Brucella abortus, Escherichia coli,* foot and mouth disease virus, rabies virus, vaccine virus, *Dermacentroxenus rickettsiæ.*
Sheep. *Bacillus anthracis, Clostridium œdematis-maligni, Clostridium welchii, Escherichia coli, Pasteurella pestis(?), Pasteurella tularensis,* foot and mouth disease virus, Rift Valley fever virus, vaccine virus, *Dermacentroxenus rickettsiæ.*
Caribou: Vaccine virus.
Deer: Foot and mouth disease virus, *Dermacentroxenus rickettsiæ.*

[1] Staphylococci and *Streptococcus pyogenes* can probably be found in, or on, all animals listed.

Pig: *Brucella abortus, Clostridium novyi, Escherichia coli, Hemophilus influenzæ(?), Mycobacterium tuberculosis hominis, Salmonella suipestifer*, foot and mouth disease virus, rabies virus, vaccine virus, *Borrelia minus.*

Horse, Mule, Ass: *Clostridium histolyticum, Clostridium novyi, Clostridium œdematis-maligni, Clostridium tetani, Clostridium welchii, Escherichia coli, Loefflerella mallei, Bacillus anthracis, Mycobacterium tuberculosis bovis*, rabies virus, vaccine virus, *Dermacentroxenus rickettsiæ.*

Bat: Rabies virus.

Squirrel—Common: *Dermacentroxenus rickettsiæ, Borrelia minus.*

Ground squirrel: (*Spermophilus* seu *Citellus beechyi*): *Pasteurella pestis, Pasteurella tularensis, Dermacentroxenus rickettsiæ.*

Chipmunk: *Dermacentroxenus rickettsiæ.*

Suslik: (*Spermophilus rufescens*): *Pasteurella pestis.*

Cavy: *Pasteurella pestis.*

Gerbille: *Pasteurella pestis.*

Tarbagan: (*Arctomys bobac*): *Pasteurella pestis.*

Rat: (*Rattus ratus, R. norvegicus*): *Pasteurella pestis, Salmonella enteritidis, Borrelia minus.*

Wild: *Leptospira ictero-hæmorrhagica.*

Water: *Rickettsia nipponica, Pasteurella tularensis.*

Wood: *Dermacentroxenus rickettsiæ.*

Muskrat: *Pasteurella tularensis.*

Mice: *Bacillus anthracis, Klebsiella rhinoscleromatis, Salmonella ærtrycke, Salmonella enteritidis, Salmonella typhi-murium, Dermacentroxenus rickettsiæ, Rickettsia nipponica*, (in *Microtus montebelloi*), *Borrelia minus, Leptospira hebdomadis* (*Microtus montebelloi*), *Leptospira icterohæmorrhagica.*

Guinea-pig: *Klebsiella rhinoscleromatis, Mycobacterium tuberculosis bovis, Pasteurella pestis*, foot and mouth disease virus, *Borrelia minus.*

Rabbit: *Bacillus anthracis, Mycobacterium tuberculosis bovis, Pasteurella tularensis, Salmonella enteritidis, Salmonella ærtrycke*, foot and mouth disease virus, vaccinia virus, *Dermacentroxenus rickettsiæ.*

Opossum: *Pasteurella tularensis.*

Bandicoot: *Borrelia minus.*

Canary: Psittacosis virus.

Cockatoo: Psittacosis virus.

Parrakeet: Psittacosis virus.

Grouse: *Pasteurella tularensis.*

Carp: *Klebsiella rhinoscleromatis.*

Mosquito—*Aëdes ægypti:* Yellow fever virus, dengue fever virus.

Aëdes albopictus: Dengue fever virus.

Aedes scapularis, A. luteocephalus: Yellow fever virus.

Culex quinquefasciatus: Dengue fever virus.

Fly—Deer fly: *Pasteurella tularensis.*

Common (*Musca domestica, M. stabulans*): *Eberthella typhi, Shigella dysenteriæ* var., *Flexner*, var. *Shiga-Kruse*, var. *Sonne* (Duval), *Vibrio choleræ*, Variola virus, *Treponema pertenuis, Bacillus anthracis.*

Sandfly (*Phlebotomus papatassi*): Pappataci fever virus, *Bartonella bacilliformis(?).*

Flea (*Xenopsylla cheopis*): *Pasteurella pestis, Rickettsia prowazeki.*

Louse (*Pediculus humanus* var. *corporis*): *Rickettsia prowazeki, Rickettsia quintana, Borrelia recurrentis* var. *novyi*, etc.

Bedbug (*Cimex lectularis*): *Mycobacterium lepræ(?), Borrelia recurrentis* (European).

Cockroach: *Escherichia coli, Mycobacterium lepræ(?), Vibrio choleræ.*

Tick—Dog (*Dermacentor variabilis*): *Pasteurella tularensis, Dermacentroxenus rickettsiæ.*
House (*Ornithodorus moubata, O. talaje*): *Borrelia recurrentis* var. *duttoni.*
Wood (*Dermacentor andersoni*): *Pasteurella tularensis, Dermacentroxenus rickettsiæ.*
Rabbit (*Hemophysalis leporis-palustris*): *Pasteurella tularensis.*
Mite (*Trombicula akamushi, T. delhiensis*): *Rickettsia nipponica.*

Host and parasite specificity cannot be determined by analysis of this list because the appearance of a bacterium under a single animal species does not imply that the animal host is necessary to its existence. Also, a bacterial organism shown as a parasite of multiple animal species may be entirely non-pathogenic to any one or all of the animals in which it has been found. For information on the adaptive relationships between animal hosts and their parasites and the general biologic principles involved, the reader is referred to other sources. (Hull, T. G., Diseases Transmitted from Animals to Man, 1930; Meyer, K. F., Newer Knowledge of Bacteria and Immunology, 1928.)

Not all bacteria require a lower animal host, and many bacteria, viruses and spirochetes in the above list may be found in nature on non-living media. Wherever there exists a possibility that a parasite may live outside of another organism, it must either possess defences of its own or there must be necessary elements in the environment which favor its nutrition or protect it from hazardous surroundings. Again excluding those organisms which are transferred from man to man by direct contact or are transmitted by a medium on which they cannot exist for any significant length of time there remain many bacteria which can survive in air, water and soil, or on vegetation, dead animal tissues, foods, dust, débris and a multitude of inanimate objects and fomites.

Air *per se* is favorable to pathogenic bacteria only insofar as it acts as a transporting mechanism which enables the organisms to gain access to some more favorable environment. This generalization carries the danger of understating the importance of air because the organisms, especially those which invade by way of the respiratory tract, are largely dependent for survival on having some means of access to the nose and mouth of man and animals. Therefore, although these pathogens probably cannot multiply in air and only survive passage through it by virtue of spore formation or the ability to resist drying in an inactive vegetative form, the air itself, and especially moving air, is a definitely valuable ecologic factor.

Bacteria in air are free-floating suspensions usually intimately associated with other particulate matter which is itself air-borne. Because the sources from which they originate are practically never composed entirely of masses of bacteria, it probably is the rarest occurrence that a particle of bacterial suspension in air is made up solely of bacteria. There is probably always either some water,

organic or inorganic salts, or dried minutely divided materials of animal, vegetable or inorganic origin associated with them. The physical properties of the air therefore assume major importance in its value to the organism. Volume, weight, surface area and momentum in the particle and density, water-vapor, temperature and motion of the air are the principal factors that determine the length of time the particles remain in suspension and the distance they can be carried. Provided the organism can protect itself against destruction or be protected by associated enveloping or otherwise favorable media while it is being carried through the air, then the longer it remains in this state the better will be its chances of meeting up with its favorite soil, the respiratory organs of a new host. Should it fall rapidly to the ground or lodge on any other medium, its chances of survival are lessened because of the interposition of new hazards. In order now to reach its host it must again be taken into the air as a component of dust or gain access to the nose or mouth of a favorable animal at an added risk through another medium of transmission.

Wells,[1] Wells and Stone,[2] and Wells and Wells[3] have made important contributions to the understanding of the mechanics of droplets and droplet nuclei as they are propelled into the air and undergo certain physical changes in their fall under the force of gravity and in air of variable physical characteristics. Correlated with this study are valuable observations on the viability of bacteria under these conditions. These are matters of tremendous epidemiologic *significance because they involve fundamental principles in the dis*semination of air-borne bacteria which are living, infectious, and made available to new hosts by rapid and widespread transportation.

A colony of pathogenic bacteria can maintain itself best, by growth and reproduction, at a temperature of 37° C. (98.6° F.) which is human body heat. At this *optimum* temperature their rate of multiplication and the accumulation of inhibitory substances in the growth medium bear the most favorable relationship to each other and to the "normal" growth curve of the colony. For the individual organism, a higher temperature may favor more rapid reproduction, but this apparent benefit is not necessarily beneficial to the colony. Outside the body of man or animals the optimum temperature plays little part because most pathogenic organisms do not grow and multiply under the ordinary external environmental conditions. It is only when they meet with some very favorable organic *medium suited to their species (which is a relatively rare occurrence)* and from which they can obtain nutrient, that an optimum temperature is of beneficial significance.

[1] Wells, W. F.: Am. Jour. Hyg., 20, 611, 1934.
[2] Wells, W. F., and Stone, W. R.: Am. Jour. Hyg., 20, 619, 1934.
[3] Wells, W. F., and Wells, M. W.: Jour. Am. Med. Assn., 107, 1698, 1936.

Extremes of temperature are highly unfavorable to all bacteria. Short of the extremes there are high and low points at which bacteria die under different conditions and length of exposure. The *thermal death time* of a species of bacteria is the time required to kill the organism at a given temperature or range of temperature. The temperature chosen is arbitrary and selected in accordance with the most practical use to which the knowledge gained is to be put. For example, milk is readily sterilized by pasteurization at 63° C. (145° F.) for thirty minutes, its thermal death time at this temperature. It would be impractical to know that sterilization could be accomplished in three or four hours at a lower temperature.

The following part-table from Gay shows the resistance of various organisms to heat in the order of increasing resistance:

Treponema pallidum	*Escherichia coli*
Neisseria gonorrhœæ	*Mycobacterium tuberculosis*
Diplococcus pneumoniæ	*Escherichia coli* (some strains)
Corynebacterium diphtheriæ	*Brucella abortus*
Bacillus anthracis	*Bacillus anthracis* spores
Streptococcus pyogenes	*Bacillus subtilis* spores
Eberthella typhi	*Clostridium botulinum* spores
Staphylococcus aureus	

Most bacteria can survive long periods at temperatures as low as 5° to 10° C. (41° to 50° F.) and some (*Eberthella typhi*) can live in ice. At these temperatures metabolism is practically at a standstill.

Water (moisture) is an essential to vegetative activity of all bacteria. While some vegetative forms and spores may be relatively resistant to drying the presence of moisture always acts in favor of survival. It not only supplies fluid for the bacterial body but acts as a solvent, diluent and menstruum for nutrients, and favors the availability of these essentials for vital activity of the organism. Milk, dilute feces, moist animal matter and water containing organic matter, most often supply the most favorable media for growth and multiplication (at times) of pathogenic organisms in their passage from man to man. Moist secretions, excretions, and discharges can maintain the viability of organisms under conditions of exposure that would otherwise be fatal.

Watery media in general are favorable to the transmission of viable pathogens, and present an important channel by which they can be returned to the animal body. It is probably no coincidence that the most common water-borne organisms are the pathogens which gain entry through the alimentary tract and produce diseases of this system and are disseminated through discharges from it.

All of the pathogenic bacteria require preformed organic substances of either animal or vegetable origin. The different species and even varieties vary greatly in their quantitative and qualitative

requirements of these materials. These specific differences cannot be taken up in this work, but it must be pointed out that the more nearly the environment comes to supplying the full quota of the specific nutrients, the more favorable it will be to the normal activity of the organisms. Food and food débris, alvine and other discharges, dead or living animal and vegetable matter, supply such essentials for many of the important human pathogenic bacteria and make these substances of paramount epidemiologic importance.

The presence of free oxygen in the environment is essential to some bacteria, detrimental to others and a matter of indifference to many. The *aërobes* are those which live in the presence of free oxygen and *anaërobes* are inhibited by it. There are some organisms which thrive as aërobes, but also possess the faculty of adjusting themselves to the anaërobic condition. These are the *facultative anaërobes*. Conversely, organisms which live readily as anaërobes may, in some instances, adapt themselves to a free oxygen environment (*facultative aërobes*). Most of the human pathogens are aërobic. When they can live only in free oxygen they are called *obligate aërobes*. The following are anaërobic pathogenic organisms for which the absence of free oxygen is obligatory (*obligate anaërobes*): *Clostridium tetani, Clostridium œdematis-maligni, Clostridium botulinum.* All others do best in the presence of free oxygen or can adapt themselves to it.

Obviously the presence or absence of free oxygen in a medium in which an organism's lot happens to fall after it has left the animal body will determine in many instances whether it lives or dies. *Anaërobic bacteria find their greatest opportunities for growth in* the interior of dead organic matter. (Most of these form spores and can persist in soil for long periods of time.)

The viruses (if they are living disease agents) can live and multiply only in living cells; those which are pathogenic to man only in animal cells. Little is known of their survival outside of the body, but epidemiologic studies in the field and laboratory have shown that they can be transmitted through air and some liquid media (rabies virus in saliva).

The *Rickettsiæ* grow best at temperatures near 30° C. (86° F.) under aërobic conditions and in the presence of living cells. Nothing is known of their presence outside of animal bodies except under experimental *in vitro* conditions.

FUNGI.

The majority of pathogenic fungi show selectivity in the tissues of the human host. Most of them thrive best on the external surfaces of the body where they are subjected to changing environmental conditions against which they receive but little protection

from the host. That which the host has to offer is largely of the nature of nutrient and a certain degree of warmth and moisture. Some invade the skin and its appendages more deeply, so that they have the added advantage of protection and nutrition by the cells of the host. A few are able to grow in the contents of hollow viscera and occasional types within such tissues as the liver, lungs and brain.

Knowledge of the epidemiology of the fungi is so meager that few positive statements with regard to their loci in nature can be made. In the list of the organisms dependent solely on man (see page 412) it has been necessary, in the case of the fungi, to query the definiteness of the assumption. It is probable, however, that in most of them at least the vegetative forms are limited to man, whereas their spores may exist on inanimate environmental materials. This in actuality comes to the same thing as saying that they are dependent solely on man for growth and reproduction. Man, then, in these instances is an essential factor in their ecology, and the survival of the fungus race will depend on the availability of this host, at least under their present state of adaptation.

While direct intimate contact of one human with another human infected host is the usual means of transmission of these fungus diseases, their survival is greatly enhanced by their temporary freedom from the body as resistant vegetative forms or spores in scales, crusts, discharges, shed hairs, sputum, abraded skin particles, nail peelings, and sweat.

Animal hosts other than man are known in the case of some of the microsporons and trichophytons. No reliability can be placed on the inference that either man, or the animal, is an essential host, in the sense of being definitive, as is the case with some bacteria and protozoa. Although a small minority produce natural disease in animals it is too early to assume that these are the all-important reservoirs for the fungi concerned. The ability to persist on animal tissues in a form in which they can be spread to man will certainly supplement their chances of survival outside of man.

Animal Hosts (Natural) of Pathogenic Fungi.

Animal origin probable—host not determined: *Trichophyton album, T. farinulentum, T. lacticolor, T. ochraceum, T. persicolor, T. radiolatum.*
Cat: *Trichophyton felineum.*
Dog: *Trichophyton mentagrophytes, Microsporum lanosum.*
Cattle: *Trichophyton mentagrophytes, T. felineum.*
Sheep: *Trichophyton mentagrophytes, T. felineum.*
Pig: *Trichophyton mentagrophytes, T. felineum.*
Horse: *Trichophyton equinum, T. mentagrophytes, T. felineum, T. granulosum, Sporotrichum beurmanni.*
Mouse: *Microsporum fulvum.*
Birds: *Achorion gallinæ, Microsporum lanosum.*
  Fowl: *Trichophyton megnini.*
  Pigeon: *Trichophyton megnini.*

The optimum temperature and the growth temperature range of the fungi fall well within the environmental temperature of man under most living conditions. *Epidermophyton* and *Ectothrix* grow best at 25° C. (77° F.) and *Endodermophyton* at 26° to 27° C. (80° to 85° F.). Nevertheless it can be stated with some assurance that a high average outside temperature is more favorable to fungus growth and reproduction than low temperatures. If all other factors are relatively equal, this probably explains the higher prevalence of the epidermophytoses and trichophytoses in hot climates. In colder regions this warmth (and added moisture) is attained by the retention of body heat beneath clothing.

Moisture is essential to the vegetative stages of fungi, and wherever it is present acts in favor of growth and survival. This may be true of some fungi even outside of the animal body in which instances some growth and multiplication may take place on inanimate objects. In general, soil and decaying vegetable and animal matter are likely to supply the most favorable medium because of the presence in them of preformed nutrients, particularly carbohydrates. The apparent ease with which some fungi appear to be picked up from earth, and the handling of animal and plant products may be due to the mycelial threads already there.

All pathogenic fungi are obligate aërobes and cannot make direct use of atmospheric CO_2.

PROTOZOA.

The pathogenic protozoa are highly parasitized members of their class and for the most part depend on animal hosts. Although only one (*Trypanosoma braziliensis*) is known only in man it is probable that all are highly dependent on the human host for continued existence of the species. *Isospora* and *Sarcocystis* are found outside of man, and one of them (*Sarcocystis*) is a parasite of many animal species, so it is possible that their need for man is far less than is the case with others.

The members of the genera *Leishmania, Plasmodia* and *Trypanosoma* exhibit what might be called a "closed" parasitism in the sense that at no time or stage in their life cycle are they ever brought into the open environment. They are transmitted to the human by inoculation and are taken from him through the hypodermic route and pass through all other developmental stages within the bodies of their animal hosts. Probably twelve out of these fourteen pathogens would fail to survive under their present state of adaptation if man were removed from their environment.

Because the *Leishmania, Plasmodia* and *Trypanosoma* undergo special forms of reproduction and development within animals other than man, these lower forms are of great importance to them. This

is especially true of the *Plasmodia*, which undergo their sexual cycle in the mosquito.

Ecologically, the continued existence of these protozoa in any single locality is a highly problematic affair.

Sarcocystis lindemanni also lives a closed existence in the muscles of its human and animal hosts. It is an example, however, of accidental parasitism in man, for he obtains it only through the ingestion of meat containing sarcocysts and is himself unable to pass them on because they develop in his own muscles (provided they excyst and penetrate his intestinal wall) and have no further avenue of escape. The human host in this instance may be beneficial to the individual generation of Sarcocystis concerned, but 100 per cent fatal to the perpetuation of the race through man.

The degree of susceptibility of the human to these parasites is probably of considerable importance, but to far less extent than with the bacteria. Insofar as this permits their invasion and multiplication, it is a factor in survival. The parasites of malaria reveal more dependence on this factor than the others, although there is evidence that lowered resistance is seen to *Endameba* and *Trypanosoma*. Lowered resistance to *Trypanosoma brucei* is believed by some to permit this organism, ordinarily found only in cattle, to become pathogenic for man.

Animal Hosts (Natural) of Pathogenic Protozoa.

Cat: *Endamœba histolytica(?)*.
Dog: *Endamœba histolytica(?)*.
Cattle: *Sarcocystis hominis*.
Sheep: *Sarcocystis hominis*.
Pig: *Sarcocystis hominis, Balantidium coli*.
Bat: *Trypanosoma cruzi*.
Rat: *Sarcocystis hominis, Endamœba histolytica*.
Mice: *Sarcocystis hominis*.
Armadillo: *Trypanosoma cruzi*.
Opossum: *Trypanosoma cruzi*.
Mosquito (*Anopheles quadrimaculatus, A. maculipennis, A. hyrcanus*): *Plasmodium falciparum, P. malariæ, P. vivax*. (Other species of anopheles are of great importance in special geographic regions and to different strains of plasmodia.)
Tsetse-fly (*Glossina palpalis*): *Trypanosoma gambiense*.
(*Glossina morsitans*): *Trypanosoma rhodesiense*.
Sandfly (*Phlebotomus chinensis*): *Leishmania donovani*.
(*Phlebotomus sp.?*): *Leishmania tropica(?)*.
Bug (*Panstrongylus (Triatoma) megistus*): *Trypanosoma cruzi*.

Other environmental factors are of importance only to those members of the class which escape from the animal through discharges from the intestinal canal where they have been living. With them, the factors of temperature and moisture are paramount. Free-living forms of *Balantidium coli, Endamœba histolytica, Isospora hominis*, and *I. belli* cannot survive more than a few hours or days

in passed feces and depend for survival over the period while waiting to be taken up by a new host on their power to form more or less resistant cysts. Since only the cysts are infective for man, cyst formation becomes a necessary defense mechanism.

The evidence that *Trypanosoma gambiense* can complete its life cycle in the tsetse-fly only at temperatures from 22° to 24° C. (70° to 75° F.) shows that even protozoa living entirely within animal bodies are not completely independent of external environmental factors. The positive side of this picture may point to the need for further study on the influence of temperature changes on parasites within cold insect hosts and the advantages to them of optimal outside conditions.

HELMINTHS.

None of the pathogenic helminths are with any degree of certainty so dependent on man alone that they are not exposed to other ecologic factors in some stage of their existence. *Gastrodiscoides hominis* appears on the list of organisms solely dependent on man (page 412) only for the reason that it is so far unknown outside of the human body. *Demodex folliculorum* has, in addition, the strong suspicion that it plays no part, or very little, in the pathogenesis of the comedo lesions in which it is found. On the other hand, the necessity of human parasitism to most of the helminths is of a high order, and in some assumes an absolute degree (obligate human parasites) for the completion of their life cycle. The value of the human host to the parasite is therefore relative between the different organisms as they show variable degrees of dependence on man. As with organisms in other classes of the parasites many could not exist without an available human in which to carry on their development.

Resistance of the host, in the sense of immunity (other than species immunity) is of relatively little moment to the helminths. Although some possess antigenic powers, the antibody reactions of the host are generally weak and ineffectual.

The highly developed specializations in structure and functions of these multicellular organisms is correlated with specialization in the selection of suitable environments for their adaptation within the host. All show special predilections for rather limited anatomic sites which must depend almost entirely on their genetic potentialities. As a result they must be able to satisfy these requirements or perish. They are effectively restricted in the first place by the portal of entry and show little, if any, ability to enter by alternate routes, and even when they have once gained admission to the human body must pass several hazards before they reach the place most suited to further development.

The circuitous routes taken by the migrating larvæ of *Ancylostoma* and *Ascaris* are cases in point. Such bizarre wanderings subject the immature parasites to serious obstacles such as lymph channels and capillaries too small to accommodate them, highly acid and enzyme-inhibiting gastro-intestinal secretions, loss from the host by fortuitous circumstances surrounding the arrival of the parasite in an organ communicating with the exterior, and various physiologic states and stages of activity in the tissues and organs of the host. But for these, probably many light infections in the human would be heavy and of far more serious consequences.

Slightly less than one-half of the pathogenic helminths inhabit man as the only alternate to some definitive host. The survival of their species can be accomplished without man, therefore, so long as the alternate hosts are available. Nevertheless, the social conditions under which man lives and his habits and customs frequently make it easier and more valuable to the parasite to propagate through man. This is especially true in the case of the flukes which are disseminated largely through environmental channels where man is constantly placing himself in their path.

The relationship between the helminths and the lower animals is quite similar to that with man. These animals act as intermediate and definitive hosts and permit the survival of the parasite race through their accommodations to them. In the case of *Echinococcus granulosus* and *Ancylostoma braziliense*, the lower animals possess the entire responsibility for their survival because the lower animals in these instances are the only definitive hosts and man plays the part of intermediate host. *Trichinella spiralis* undergoes its definitive and intermediate development in either man or animals.

Animal Hosts (Natural) of Pathogenic Helminths.

Monkey: *Echinococcus granulosus* larvæ.
Leopard: *Echinococcus granulosus* larvæ.
Wildcat: *Clonorchis sinensis.*
Cat: *Echinococcus granulosus, Clonorchis sinensis, Ancylostoma braziliense, Heterophyes heterophyes, Opisthorchis felineus, Trichinella spiralis* larvæ.
Civet cat: *Opisthorchis viverrini.*
Dog: *Ancylostoma braziliense, Clonorchis sinensis, Dioctophyme renale, Echinococcus granulosus, Heterophyes heterophyes, Opisthorchis felineus, Tænia solium* larvæ, *Trichinella spiralis* larvæ.
Wolf. *Dioctophyme renale.*
Jackal: *Echinococcus granulosus.*
Fox. *Heterophyes heterophyes, Trichinella spiralis* larvæ.
Mink: *Clonorchis sinensis.*
Marten: *Clonorchis sinensis, Dioctophyme renale, Trichinella spiralis* larvæ.
Badger. *Clonorchis sinensis.*
Otter: *Dioctophyme renale.*
Bear: *Trichinella spiralis* larvæ.
Raccoon. *Dioctophyme renale*
Coati: *Dioctophyme renale.*
Seal: *Dioctophyme renale.*
Llama: *Fasciola hepatica, Tænia saginata* larvæ.

Camel: *Fasciola hepatica, Echinococcus granulosus* larvæ.
Giraffe: *Echinococcus granulosus* larvæ, *Tænia saginata* larvæ.
Cattle and oxen: *Dioctophyme renale, Fasciola hepatica, Echinococcus granulosus* larvæ, *Tænia saginata* larvæ.
Buffalo: *Fasciola hepatica, Tænia saginata* larvæ.
Goat: *Fasciola hepatica, Echinococcus granulosus* larvæ, *Tænia solium* larvæ.
Sheep: *Fasciola hepatica, Echinococcus granulosus* larvæ, *Tænia solium* larvæ.
Pig: *Clonorchis sinensis, Fasciola hepatica, Fasciolopsis buski, Echinococcus granulosus* larvæ, *Tænia solium* larvæ, *Trichinella spiralis* larvæ.
Wild boar: *Trichinella spiralis* larvæ.
Horse: *Dioctophyme renale, Fasciola hepatica, Echinococcus granulosus* larvæ.
Tapir: *Echinococcus granulosus* larvæ.
Elephant: *Fasciola hepatica.*
Squirrel: *Echinococcus granulosus* larvæ.
Mouse: *Hymenolepis nana.*
Field mouse: *Schistosoma japonicum.*
Rat: *Hymenolepis nana, Trichinella spiralis* larvæ.
Guinea-pig: *Clonorchis sinensis.*
Rabbit: *Echinococcus granulosus* larvæ
Fish (*Percidæ, Gobiidæ, Abantinidæ*): *Clonorchis sinensis cercariæ.*
(*Idus Idus*): *Dioctophyme renale* cercariæ(?).
(Pike, perch, salmon, trout, lake trout, rainbow trout, grayling, Miller's thumb, sandpike, walleye, burbot, barbel): *Diphyllobothrium latum* sparganum.
Mosquito (*Culex fatigans, C. pipiens, Aëdes ægypti, A. variegatus, A. togoi, Mansonia pseudotittilans, M. uniformis, Anopheles albimanus, A. rossi, A. costalis, A. algeriensis, A. nigerrimus*): *Wuchereria bancrofti* microfilaria.
Fly (*Chrysops dimidiata* (mango fly), *C. silacea*): *Loa loa* microfilaria.
Gnat (*Similium damnosum*): *Onchocerca volvulus* microfilaria.
Crab and crayfish (*Astacus japonicus, A. similis, Eliocheir japonicus, E. sinensis, Potamon dehaani, P. obtusipes, Parathelphusa sinensis, Sesarma dehaani, Pseudothelphusa iturbei*): *Paragonimus westermani* cercariæ
Cyclops (*Cyclops brevispinosus, C. prasinus, Diaptomus gracilis, D. oregonensis*): *Diphyllobothrium latum* procercoid larvæ.
(*Cyclops quadricornis, C. strenuus, C. viridis, C. bicuspidatus*): *Dracunculus medinensis* larvæ.
Snail (*Parafossarulus striatulus, Bithynia fuchsiana, B. longicornis*): *Clonorchis sinensis* ova.
(*Melania libertina, M. multicincta, M. nodiperda, M. obliquegranosa, M. paucicincta, M. tuberculatus*): *Paragonimus westermani* cercariæ.
(Spp.?): *Echinostoma ilocanum.*
(*Bullinus dybowski, B. contortus, B. innesi, Physopsis africana, Planorbis metidjensis* var. *dufouri*): *Schistosoma hematobium* cercariæ.
(*Katayama nosophora, Oncomelania hupensis, K. formosana*): *Schistosoma japonicum* cercariæ.
(*Planorbis boissyi, P. pfeifferi, Physopsis africana, Planorbis sudanicus, P. olivaceus, P. centrimetralis, P. guadeloupensis*): *Schistosoma mansoni* cercariæ.
(*Limnea* spp., *Ampullaria luteastoma, Isidora tropica, Limnea viatrix*): *Fasciola hepatica* cercariæ.
(*Planorbis cœnosus, Segmentina nitidella, S. schmackeri, S. hemisphærula*): *Fasciolopsis buski* cercariæ.
(*Mugil cephalis*): *Heterophyes heterophyes* larvæ.

The only human helminths which live a completely closed parasitic life in an animal body are the autoinfective generations of *Enterobius vermicularis* and *Hymenolepis nana.* The nearest approach to this state in the remainder of these parasites is found in *Loa loa, Onchocerca volvulus* and *Wuchereria bancrofti*. In these the parasite is taken up directly by the biting insect and carried in its body for a time and then deposited on the skin of the new host during the act of biting. The microfilaria remain on the skin so short a time that they are subjected to little environmental hazards other than the danger of being brushed off or washed away before they have had an opportunity to penetrate the skin.

All other helminths possess some one or more stages outside of animal hosts during which their survival is imperiled. These stages are represented by eggs or free-living larval and developmental forms (miracidia and cercariæ).

Helminths Which Liberate Eggs Into the External Environment.

Ancylostoma braziliense	*Heterophyes heterophyes*
Ancylostoma duodenale	*Hymenolepis nana*
Ascaris lumbricoides	*Necator americanus*
Clonorchis sinensis	*Opisthorchis felineus*
Dioctophyme renale	*Opisthorchis viverrini*
Diphyllobothrium latum	*Paragonimus westermani*
Diphyllobothrium mansoni	*Schistosoma hematobium*
Dracunculus medinensis	*Schistosoma japonicum*
Echinococcus granulosus	*Schistosoma mansoni*
Echinostoma ilocanum(?)	*Strongyloides stercoralis*
Enterobius vermicularis	*Tænia saginata*
Fasciola hepatica	*Tænia solium*
Fasciolopsis buski	*Trichocephalus trichiuris*
Gastrodiscoides hominis(?)	

The concentrated, undiluted fecal mass is unfavorable for the development and hatching of the eggs of *Ancylostoma, Necator, Ascaris, Clonorchis, Fasciola, Fasciolopsis, Schistosoma mansoni,* and *Trichocephalus.* Acidity, lack of oxygen, and the action of bacteria are the primary factors involved. Subsequent dilution with water even after several weeks permits those which have survived actual destruction and death of the embryo to become active and hatch. The eggs of *Trichocephalus trichiuris* are highly resistant to drying and oxygen lack and remain viable for months or years.

Excess water is highly unfavorable to the further growth of the embryo in *Ancylostoma* and *Necator* eggs, but favorable to those of *Schistosoma japonicum* and *S. mansoni, Fasciola* and *Fasciolopsis.*

The ova of *Ancylostoma* and *Necator* are killed by excessive sunlight and highly saline media.

Diphyllobothrium eggs are highly resistant to all external influences.

Helminths With Free-living Larvæ in Soil and Water.

Soil.	Water.
Ancylostoma braziliense	*Dioctophyme renale*
Ancylostoma duodenale	*Clonorchis sinensis*
Necator americanus	*Diphyllobothrium latum*
Echinococcus granulosus	*Dracunculus medinensis*
Hymenolepis nana	*Opisthorchis felineus(?)*
Strongyloides stercoralis	*Opisthorchis viverrini(?)*
Trichocephalus trichiuris	
Trichinella spiralis	

These larvæ can survive in their opposite media for limited lengths of time, but while there have less chance of meeting a favorable host.

Helminths With Free-living Miracidia and Cercariæ in Water.

Fasciola hepatica	*Fasciolopsis buski*
Paragonimus westermani	*Schistosoma japonicum*
Schistosoma hematobium	*Schistosoma mansoni.*

Drying is fatal to the larvæ of all of these species. A certain amount of moisture in the soil is necessary for the larvæ living best in that medium, and the *miracidia* and *cercariæ* of the water forms must have sufficient water in which to swim to their intermediate hosts. Flood water is also a hazard to all forms, for the soil-living larvæ are then forced into their less favorable medium and the probability of the water forms being able to complete their life cycle is dangerously lessened.

With the exception of *Strongyloides stercoralis* which can interpolate a new generation in the free-living stage the members of the above two lists must find a new host within a relatively short period of time or die out. In the meantime they are subject to the possibility of destruction by other animals. Summing up all of the hazards in the interval between host and host, the free-living existence is extremely precarious and probably few of the total number which are hatched successfully ever reach a new host and complete their life cycle even that far.

Many of the lower forms of animals which act as intermediate hosts are also open to destruction by adverse circumstances in their environment. This applies to the hosts not only of the "open" types of parasites but also to those whose whole existence is spent within a host. The ecology of the hosts is too large a subject for more discussion in this work, but a knowledge of these animal relationships is essential to an understanding of the epidemiology of the helminths.

ARTHROPODS.

Among the arthropods, *Cimex lectularis*, *Cimex hemipterus*, *Pediculus humanus*, *Phthirius inguinalis*, *Pulex irritans*, *Sarcoptes scabiei*, *Demodex folliculorum(?)* and some of the mosquitoes, are the only

members which show any real specific adaptations to the human host. All of the others can and most often do live entirely independently of man. When they parasitize the human they do so accidentally and succeed in their parasitism because the materials and tissues of the host which they invade are similar enough to those of their natural habitat to furnish satisfactory nutritive media. This is particularly true of the parasitizing flies whose larvæ develop in the contents of the intestinal canal, accessory sinuses, nose, eye, ear and open wounds on the skin, and the biting insects which can utilize human blood.

These remarks do not imply that the parasites are only saprophytic. On the contrary, the developing larvæ and imagos possess certain vital processes to be considered later which are distinctly harmful to the host.

Phthirius inguinalis, *Pediculus humanus capitus* and *Sarcoptes scabiei* are the only arthropods whose whole life cycle can be carried on completely on the tissues of man. Their eggs hatch and the larvæ develop on or in the skin or hair and the adults reproduce in the same location. At times the adults may become attached to clothing and be temporarily removed from human contact.

Pediculus humanus corporis and *Pulex irritans* carry out their cycle on clothing and attach themselves to the skin only during the act of biting either as larvæ or adults.

Still farther removed from man are *Cimex lectularis* and *Cimex hemipterus*, which breed in localities inhabited by man and in close proximity to him. They live almost entirely on human blood but are attached to man only while obtaining this nourishment.

The mosquitoes, especially the domestic varieties, can and do utilize animal blood, but appear to prefer man when he is available. This may be a specific adaptation correlated with their breeding habits. They are therefore relatively dependent on man.

Ticks and mites do not require human hosts. That they ever occur on man is accidental in that he has placed himself in their way at a time when they required a blood-meal.

The biting flies (*Glossina*) probably use wild or domestic animals under most conditions, but bite man at times and become dependent on him only to the extent to which man is the more available host.

For a review of the common habitations of these occasional parasites the reader is referred to the list of their environmental loci on page 407 ff.

The eggs and larvæ of the group most intimately confined to man are destroyed by high temperatures (70° C. (158° F.) moist heat for thirty minutes; 55° C. (121° F.) dry heat for five minutes). Their optimum temperature, 32° C. (89.6° F.) is about that of the body surface under the protection of clothing. Adult *Pediculi* and

Phthirius inguinalis will desert their host during fever. They do not survive longer than three weeks on clothing removed from man.

The bedbugs (*Cimex*) can survive long periods without food, but are preyed upon in their hide-outs in cracks and crevices by red house-ants and cockroaches. All stages of the bug are instantly killed by scalding water.

The various forms of mite larvæ, while attached to and buried in the skin, are effectively protected from mechanical dislodgment. The immature forms and eggs in the soil are subject to decomposition by soil organisms and ingestion by insectivorous animals. The presence of these and adult forms on grasses, grains, fruit and vegetable products submits them to many changes in their physical environment which inhibit their development and may actually destroy them. On these locations they are easy prey to their natural enemies.

The prolonged life cycle of the tick exposes it to such a wide variety of baneful influences that they cannot be enumerated here. A point of great importance, however, is the ability of the nymph to survive the winter buried in the ground. The larvæ and adult ticks attach themselves to so many varieties of animals that there is practically always an available host.

Specific requirements among the mosquitoes determine the selection of specialized locations for oviposition and the development of larvæ and pupæ.

Anopheles requires relative still, clean natural waters in which there are water plants; *Aedes* prefers perfectly still water which may even be stagnant; *Culex* breeds in dirty and even sewage-contaminated water. *Anopheles* larvæ possess a short siphon and are, therefore, unable to develop in water with a surface film of oil which the siphon cannot penetrate.

Warmth is more favorable to the growth of the larvæ and pupæ than cold, although the eggs and larvæ can exist through a winter season and can even retain their viability after freezing.

Excess rainfall during the stage when mosquitoes are beginning to multiply in large numbers in the early warmth after winter is *detrimental to the ecologic balance between the young developmental forms and their aqueous environment.* Flooding causes their wide dispersal and a disturbance of the calm state which they prefer. A succession of light rains at the right season, on the other hand, keeps up a constant source of standing water under ideal conditions for repeated generations of new mosquitoes.

The chief natural enemy of the mosquito is the top minnow, which feeds on the insect during its aqueous stages. These and other small fish live in the still back-waters among the grasses where the mosquito is most abundant. They are mostly top feeders. The

commonest are: *Gambusia molliensa*, *Girardinus pœciloides* ("millions"), *Girardinus formosus*, *Haplochilus grahami*, *Haplochilus bifasciatus*, and other members of the genera *Cyprinodon*, *Ambassis*, *Trichogaster* and *Barbus*. Mosquito pupæ are also food for beetles, water-bugs, dragon-fly larvæ and aquatic and wading birds.

The adult mosquito can survive cold seasons of several months duration by hibernating in an inactive state in sheltered spots. The more common method of spanning the winter is by oviposition in locations where water will be assured with the return of warm weather. Larvæ, less frequently, can survive the cold if they are well protected, but pupæ cannot endure these temperatures.

Natural enemies of adult mosquitoes are the bats and other night-prowling insectivores, birds, spiders, lizards, mantids, dragon-flies and other predatory forms of small animal life.

CHAPTER XLI.

THE ACQUISITION AND PORTALS OF ENTRY OF PARASITES.

WHETHER the life history of a parasite outside of man be brief and direct or prolonged and indirect, the main interest to man is the source in the immediate environment from which he acquires it. This in no way detracts from the importance of knowing the life history of the parasite antecedent to its final approach to man, but on the contrary frequently points to one or more circumstances in the parasite's existence where it may be open to attack.

In general, parasites arrive in proximity to man as a result of their own activities (biting insects), by their transmission within or on the bodies of other organisms which carry them to man, by their presence in or on materials brought into intimate relation with their human host, or by direct contact between their human host and another one susceptible to them.

The loci in the environment of all pathogenic parasites have been noted in the systematic review in the preceding chapter. It is now possible to select those loci which are concerned with the immediate approach of the parasites to man and so arrange them as to bring together the divergent forms of organisms under their common sources. This listing is made for practical purposes in order that information may be readily available on what organisms are obtained from similar sources.

A. ORGANISMS TRANSMITTED DIRECTLY FROM MAN TO MAN.

1. **Infection of Ovum or Spermatozoön.**—Although the idea has long been held by many that the ovum can be directly infected by the spirochete of syphilis either from the maternal tissues in which the ovum developed or by impregnation by a spermatozoön bearing *Treponema pallidum* it has never been confirmed by experiment. Nor has it so far been proven impossible. Jeans[1] says, "In order to assume direct paternal transmission to the ovum, it is necessary to assume also a life cycle (of *Treponema pallidum*) in which a spore stage or something similar exists. Such an assumption is entirely unnecessary to explain the known facts and is unsupported by anything which could qualify as proof." Infection of the ovum *in situ*

[1] Jeans, P. C., in Brennermann's "Practice of Pediatrics," 2, 26, 1936.

rests on much more reasonable grounds, but this too needs confirmation.

No other infectious or parasitic agents of disease are believed to be borne by the germ-plasm in man.

2. **Transplacental Infection.**

Bacillus anthracis—one case reported.
Mycobacterium tuberculosis—rarely.
Mycobacterium lepræ—rarely, if at all.
Pasteurella pestis—unknown organisms causing endocarditis.
Treponema pallidum.
Borrelia recurrentis.
Smallpox virus.
Measles virus(?).
Mumps virus.
Yellow fever virus.
Plasmodia of malaria. Generally conceded to be possible if there is an abnormal breach in the placenta.
Schistosomes.
Leishmania donovani.[1,2]
Trypanosomes(?).
Ancylostoma and Necator —wandering larvæ.
Ascaris lumbricoides[3]—wandering larvæ.

The placenta is an efficient filter against most organisms circulating in the maternal blood. It appears that only tissue invaders such as spirochetes and wandering larvæ can pass normal, unbroken placental barriers. The still unknown nature of the viruses makes it idle to speculate at this time on the mechanisms of their transmission to the fetus.

3. **Acquired by Immediate Contact with Human Sources.**—Although it is difficult to set up arbitrary limits which will differentiate strict contact origins of pathogenic organisms from the almost direct sources from freshly contaminated materials, it seems necessary that this be done. So much of the understanding of contact infection is owed to Chapin that there is considerable reluctance in separating his category into two divisions. Nevertheless, modern interpretations of epidemiologic phenomena must adhere closely to the facts, and these point to the necessity of distinguishing between absolutely immediate contact and relatively immediate. In this section only those organisms will be considered which are taken up by one human through intimate and direct contact with the infected parts of another.

[1] Low, G. C., and Cook, W. E. Lancet, ii, 1209, 1926
[2] Hindle, E. Proc. Roy. Soc. Med., London, 103, 599, 1928
[3] Faust, E. C., and King, E. L. Discussion in "Fetal, Newborn, and Maternal Morbidity and Mortality," Committee on Medical Care for Children, White House Conference, New York, D. Appleton-Century Company, 1933.

Acquired during birth from the birth canal.

- *Diplococcus pneumoniæ*—one of the early contaminants of the nose and throat which go to make up the normal bacterial flora of these regions.
- *Mycobacterium tuberculosis hominis*—has been reported gaining entrance through the placenta at the time of its separation.
- *Neisseria gonorrheæ*—commonly infects the conjunctiva of the new-born and is a cause of ophthalmia neonatorum.
- *Staphylococcus* spp.—original member of normal bacterial flora of skin. May infect conjunctiva and umbilicus.
- *Streptococcus* spp.—original member of normal bacterial flora of the skin. May infect conjunctiva and umbilicus.
- *Treponema pallidum*—from a fresh lesion in the mother in case where the infection is acquired so late in pregnancy that the fetus has not yet been infected.
- *Plasmodia* of malaria—may first gain entrance to the fetus at the time of separation of the placenta.

Acquired post-natally.

- *Bacillus anthracis*—direct infection from contact with malignant pustule. Surgeons, nurses, attendants.
- *Clostridium histolyticum*—from contact with gas gangrene lesions in man through open lesion in skin.
- *Clostridium novyi*—from contact with gas gangrene lesions in man through open lesions in skin.
- *Clostridium œdematis-maligni*—from contact with gas gangrene lesions in man through open lesions in skin.
- *Corynebacterium diphtheriæ*—through intimate contact as in the act of kissing.
- *Diplococcus pneumoniæ*—transference of normal flora of mouth in acting of kissing.
- *Fusiformis fusiformis*—transference from mouth to mouth through kissing.
- *Hemophilus ducreyi*—organism in soft chancre most often acquired by contact during sexual intercourse.
- *Klebsiella granulomatis*—from direct contact with lesions of granuloma inguinale, probably only through broken skin.
- *Klebsiella pneumonia*—possibility of exchange of bacterial flora of mouth in the act of kissing.
- *Loefflerella mallei*—from direct handling of human lesions.
- *Mycobacterium lepræ*—unknown. Possibly from intimate human contact, especially in children.
- *Mycobacterium tuberculosis hominis; M. t. bovis*—from contact with human skin and other lesions opening externally.
- *Neisseria gonorrheæ*—infection of mucous membranes by contact with infected mucous membranes. Sexual intercourse, perverted practices, infected material in eyes of medical attendants and others.

Pasteurella tularensis—from contact with surface lesions.

Staphylococcus spp.—human contacts after birth are constant sources of body surface contamination. May enter directly by way of skin when a breach in the skin is brought into contact with a human source.

Streptococcus erysipelatis—direct contact of broken skin with lesions of erysipelas.

Streptococcus pyogenes (vars.)—broken surface contact with suppurative lesions.

Streptococcus scarlatinæ—contact with nasal mucus and sputum-contaminated skin of a scarlet fever patient. Transference from mouth by kissing.

Foot and Mouth Disease virus—directly from human lesions.

Lymphogranuloma Inguinale virus—sexual contact.

Molluscum Contagiosum virus—directly from human lesions.

Rabies virus—bite or direct contact with saliva as in kissing in an active case.

Vaccinia virus—direct transmission by contact with lesions.

Variola virus—possibly by contact but unproven.

Varicella virus—possibly by contact but unproven.

Common Cold virus—direct contact of mouth parts with nasal discharge and sputum of active cases.

Treponema pallidum—direct contact with open surface lesions—skin; mucous membrane of genitalia, mouth, nose, anus. Most frequently by sexual intercourse, nursing infants, kissing and human bites of syphilitics.

Treponema pertenuis—direct contact with skin and mucous membrane lesions of yaws.

Treponema vincenti—transferral of normal bacterial flora of mouth in act of kissing.

Achorion schonleinii—from contact with scalp of human favus cases.

Blastomyces dermatitidis—from open skin lesions and probably only through broken skin.

Coccidioides immitis—from open granulomata and probably only through broken skin.

Endodermophyton, spp.—as far as known, only by direct contact with tinea imbricata.

Hormodendron, spp.—unknown, but probably by contact with human skin lesions.

Sporotrichum, spp.—probably only by contact with organisms in open gummatous lesions of sporotrichosis.

Actinomyces maduræ—although it is demonstrated only in man, this organism may not commonly be transmitted by direct contact with open lesions.

Enterobius vermicularis—contact source only by auto-reinfection from self-contaminated fingers.

Pediculus humanus capitis et *corporis*—head and body lice transmitted by direct contact.
Phthirius inguinalis—crab-louse transmitted by direct contact.
Pulex irritans—human flea transmitted by human contact.
Sarcoptes scabiei—itch-mite transmitted by human contact.

B. ORGANISMS ACQUIRED FROM FRESHLY CONTAMINATED SOURCES.

These sources constitute the recently contaminated fomites. The distinction between the infective materials on these and the following subdivision (old contaminations and indirect sources) rests on the state of the organisms concerned, that is, they have not undergone any changes produced by drying, spore formation, or life-cycle outside of man, and the materials on which they occur have been directly and not secondarily contaminated. The use of the word "freshly" connotes a short time interval between the moment of their contamination and their acquisition by a new host. This time interval may even be momentary, but the fact that it exists indicates the possibility that it may be prolonged to the disadvantage of the organism.

1. From Contaminated Dressings, Medical Instruments, Sick Room Supplies and Accessories.

Bacillus anthracis
Clostridium, spp.
Corynebacterium diphtheriæ
Eberthella typhi
Escherichia coli
Klebsiella granulomatis
Loefferella mallei
Mycobacterium tuberculosis, vars.
Neisseria gonorrheæ
Pasteurella tularensis
Pasteurella pestis
Salmonella paratyphi
Staphylococcus, spp.
Streptococcus pyogenes
Streptococcus erysipelatos
Vibrio choleræ
Foot and Mouth Disease virus
Smallpox virus
Treponema pallidum
Treponema pertenuis
Blastomyces dermatitidis
Madurella mycetoma
Sporotrichum, var.
Leishmania tropica

2. From Contaminated Bedding, Toilet Articles, Handkerchiefs, Eating Utensils, Towels, Toothbrushes, Lipsticks, etc.

Corynbebacterium diphtheriæ
Eberthella typhi
Mycobacterium tuberculosis, vars.
Neisseria gonorrheæ
Pasteurella pestis
Shigella dysenteriæ, vars.
Staphylococci, vars.
Streptococcus pyogenes
Streptococcus erysipelatos
Streptococcus scarlatinæ
Vibrio choleræ
Monilia albicans
Smallpox virus
Varicella virus
Common Cold virus
Mumps virus
Treponema pallidum
Treponema pertenuis
Treponema vincenti
Achorion schönleinii
Epidermophyton inguinale
Microsporon, vars.
Trichophyton, vars.

3. From Contaminated Personal Articles: Books, Toys, etc.

Corynebacterium diphtheriæ
Streptococcus scarlatinæ
Smallpox virus
Common Cold virus
Mumps virus
Treponema pallidum
Others from list No. 2 far less commonly.

4. From Articles Used by the Public: Toilets, Common Cups, Eating Utensils, Public Baths.

Mycobacterium tuberculosis, vars.
Neisseria gonorrheæ
Streptococcus erysipelatos
Common Cold virus
Trichophyton, vars.
Treponema pallidum
Treponema vincenti
Molluscum contagiosum virus
Monilia albicans

5. From Contaminated Articles of Clothing.

Eberthella typhi
Loefflerella mallei
Neisseria gonorrheæ
Shigella dysenteriæ
Staphylococcus, var.
Streptococcus pyogenes
Streptococcus erysipelatos
Vibrio choleræ
Smallpox virus
Common Cold virus
Treponema pallidum
Treponema pertenuis
Epidermophyton inguinalis
Pediculus humanus capitis
Pediculus humanus corporis
Phthirius inguinalis
Trichophyton, spp.

6. From Contaminants From Fresh Animal Sources.

Bacillus anthracis—fresh blood.
Brucella abortus—fresh blood, placenta, fetus, vaginal discharge.
Brucella mellitensis—fresh blood.
Mycobacterium tuberculosis bovis—infected udder.
Streptococcus epidemicus—infected udder.
Streptococcus scarlatinæ—infected udder.
Foot and Mouth Disease virus—animal lesions.
Rabies virus—tears, saliva, nasal discharge.
Rift Valley Fever virus—infected sheep tissues.
Verruca Vulgaris virus—infected udder(?).

7. From Contaminated Expiratory Droplets.

Corynebacterium diphtheriæ
Diplococcus pneumoniæ
Hemophilus influenzæ
Hemophilus pertussis
Klebsiella pneumoniæ
Mycobacterium tuberculosis hominis
Neisseria intracellularis
Pasteurella pestis
Pasteurella tularensis
Streptococcus epidemicus
Streptococcus scarlatinæ
Psittacosis virus
Common Cold virus
Mumps virus
Poliomyelitis virus(?)
Epidemic Influenza virus
Measles virus

C. ORGANISMS ACQUIRED FROM INDIRECT, IMMEDIATE SOURCES.

This classification includes all pathogenic organisms which can exist free in the environment or in animal hosts.

Among the bacterial organisms are all those which can resist death through relatively long periods of time. It excludes those whose existence outside of man is limited to a few hours under normal conditions. Some of these latter, however, may under very favorable circumstances resist those factors which are ordinarily rapidly fatal to them. When this is believed to be the case in any organism it will be included, but, when doubt exists, the fact will be noted with a question mark.

There is so little known about the existence in nature outside of man of many of the fungi that it has seemed wise to list only those about which some information is at hand.

Because this classification is based on the ultimate link in the natural history of parasites as they are brought finally in contact with man, the form in which they are presented at that moment must necessarily be the infective stage of the organism. This may be the egg, larva, nymph, cercaria, sparganum, cyst, spore, or the fully developed adult. For the sake of brevity the infective forms have not been repeated in this list, but the reader will find them outlined in the descriptive text under each organism in the list on page 395.

1. Entering by Way of the Skin and Superficial Mucous Membranes (Contact and Inoculation).

From dirt and soil:

Bacillus anthracis
Clostridium histolyticum
Clostridium novyi
Clostridium œdematis-maligni
Clostridium tetani
Clostridium welchii
Diplococcus pneumoniæ
Escherichia coli
Mycobacterium lepræ(?)
Leptospira icterohæmorrhagica
Coccidioides immitis
Madurella mycetoma(?)
Actinomyces maduræ(?)
Ancylostoma braziliense
Ancylostoma duodenale
Necator americanus
Strongyloides stercoralis
Cutaneous myiasis-producing flies
Leptus autumnalis
Trombicula akamushi

From growing grasses and vegetation:

Bacillus anthracis
Clostridium œdematis-maligni (fruit)
Clostridium tetani
Blastomyces dermatitidis (rotting wood)
Ornithodorus talaje
Pediculoides ventricosis (grain and straw)
Rhizoglyphus parasiticus (tea gardens)
Trombicula akamushi

From growing grasses and vegetation:—(*Continued.*)

Dermacentor andersoni
Dermacentor variabilis
Glossina palpalis
Glossina morsitans
Leptus autumnalis
Ornithodorus moubata
Trombicula schüffneri (tobacco)
Trombicula delhiensis (palm oil plantations)
Tyroglyphus longior (copra and vanilla)

From live animal sources:

Corynebacterium diphtheriæ(?) (organisms from animal sources not proven identical with human pathogens)
Loefflerella mallei (equines)
Borrelia minus (rat-bite)
Leptospira hebdomadis (mouse urine)
Trichophyton equinum (horse)
Trichophyton felineum (cat, dog, horse, cow)
Trichophyton granulosum (horse)
Leprospira icterohæmorrhagica (mouse and human urine)
Rabies virus (canines, felines and others)
Achorion gallinæ (birds)
Microsporum fulvum (mouse)
Microsporum lanosum (dog and birds)
Trichophyton mentagrophytes (horse, cow, dog, sheep)
Trichophyton megnini (fowl and pigeon)

From animal products (not taken as food):

Bacillus anthracis (hides, furs, wool, hair, etc.)
Brucella abortus (hog products)
Clostridium novyi (sausage makers and handlers of animal meat refuse)
Pasteurella tularensis (rodent and other small animal hides, pelts, fur, hair, meat, blood)
Streptococcus hemolyticus (meat handlers)
Cutaneous myiasis-producing flies (old meat, carcasses, exposed meat foods)
Rift Valley Fever virus (handling infected sheep tissues)

From contaminated bathing and washing water, field water, soil water, sewage and drain water:

Clostridium welchii
Leptospira icterohæmorrhagica
Staphylococcus, spp.
Endamæba histolytica
Schistosoma hematobium
Schistosoma japonicum
Schistoma mansoni
Ancylostoma duodenale
Necator americanus
Aëdes, spp.
Culex, spp.
Anopheles, spp.

By insect transmission:
- *Bacillus anthracis* (by blood-sucking insects?)
- *Bartonella bacilliformis* (sandfly?)
- *Escherichia coli* (flies)
- *Eberthella typhi* (flies and cockroach)
- *Mycobacterium lepræ* (bedbug? and cockroach?)
- *Pasteurella tularensis* (ticks)
- *Shigella dysenteriæ*, spp. (flies)
- *Streptococcus hemolyticus* (flies)
- *Staphylococcus*, spp. (flies)
- *Vibrio choleræ* (flies and cockroach)
- *Varicella virus* (flies and other vermin)
- Yellow Fever virus (Aëdes mosquitoes)
- Dengue Fever virus (Aëdes and Culex mosquitoes)
- Pappataci Fever virus (sandfly)
- Poliomyelitis virus (insect transmission suspected only)
- *Dermacentroxenus rickettsiæ* (ticks)
- *Rickettsia nipponica* (Japanese Kedani mite)
- *Rickettsia prowazeki* (body louse and rat flea)
- *Rickettsia quintana* (body louse)
- *Borrelia recurrentis* (ticks, bedbug and body louse)
- *Treponema pertenuis* (flies)
- *Leishmania donovani* (sandfly)
- Plasmodia of malaria (Anopheles mosquitoes)
- *Trypanosoma cruzi* (bug—*Panstrongylus megistus*)
- *Trypanosoma gambiense* (tsetse fly—*g. palpalis*)
- *Trypanosoma rhodesiense* (tsetse fly—*g. morsitans*)
- *Loa loa* (mango fly)
- *Onchocerca volvulus* (buffalo gnat)
- *Wuchereria bancrofti* (Aëdes, Culex and Anopheles mosquitoes)
- *Dermatobia hominis* (fly, tick and mosquito)

From miscellaneous contact sources:
- *Escherichia coli* (on many articles of common use)
- *Clostridium tetani* (as a contaminant of surgical catgut, umbilical cord ties, and animal vaccines and sera)
- *Clostridium welchii* (ubiquitous on many exposed articles of common use)
- *Pasteurella tularensis* (laboratory cultures)
- *Staphylococcus*, spp. (ubiquitous)
- *Streptococcus pyogenes* (ubiquitous)
- *Epidermophyton inguinale* (toilet articles)
- *Microsporon audouini* (toilet articles)
- *Microsporon furfur* (clothing)
- *Microsporon xanthoides* (toilet articles—razors)
- *Monilia albicans* (nursing bottles and nipples)

From miscellaneous contact sources:—(*Continued.*)
Trichophyton, spp. (clothing—toilet articles)
Cimex lectularis (beds, furniture and floors)
Hippelates pusio (free-flying in human habitations)
Hypoderma bovis (eggs in clothing)
Pediculus humanus corporis et *capitis* (clothing)
Phthirius inguinalis (clothing)
Pulex irritans (clothing, floors and furnishings)

2. Entering by Way of the Respiratory Tract (Air-borne in Dust or as Droplet Nuclei, Free or Attached to floating Particles. Fresh Infected Expiratory Droplets Excluded.)

Clostridium welchii
Clostridium tetani
Corynebacterium diphtheriæ(?)
Hemophilus influenzæ(?)
Klebsiella pneumoniæ(?)
Mycobacterium tuberculosis hominis
Staphylococcus, spp.
Streptococcus epidemicus
Streptococcus viridans
Variola virus(?)
Psittacosis virus
Poliomyelitis virus(?)

3. Entering by Way of the Alimentary Tract.

From contaminated fingers:
Brucella abortus
Brucella melitensis
Eberthella typhi
Escherichia coli
Mycobacterium tuberculosis hominis et *bovis*
Monilia albicans
Balantidium coli
Endameba histolytica
Isospora belli
Ascaris lumbricoides
Salmonella aertrycke
Salmonella paratyphi
Salmonella schottmülleri
Salmonella typhi-murium
Vibrio choleræ
Enterobius vermicularis
Hymenolepis nana
Leptospira icterohæmorrhagica
Strongyloides stercoralis

In drinking water and water used in the preparation of foods:
Clostridium welchii
Eberthella typhi
Escherichia coli
Salmonella aertrycke
Salmonella paratyphi
Salmonella schottmülleri
Salmonella typhi-murium
Shigella dysenteriæ, spp.
Streptococcus epidemicus
Vibrio choleræ
Endameba histolytica
Ascaris lumbricoides
Fasciola hepatica
Dracunculus medinensis
Paragonimus westermani
Schistosoma hematobium
Helophilus pendulus
Porocephalus armillatus

In milk and dairy products:

Brucella abortus
Brucella melitensis
Eberthella typhi
Mycobacterium tuberculosis hominis et *bovis*
Salmonella aertrycke
Salmonella typhi-murium
Shigella dysenteriæ, spp.
Streptococcus epidemicus
Streptococcus hemolyticus
Streptococcus scarlatinæ
Foot and Mouth Disease virus
Rabies virus
Poliomyelitis virus (suspected only)
Monilia albicans

On vegetables, fruit and salads:

Clostridium welchii
Eberthella typhi
Shigella dysenteriæ, spp.
Vibrio choleræ
Endameba histolytica
Isospora belli et *hominis*
Ascaris lumbricoides
Echinococcus granulosus
Fasciola hepatica
Fasciolopsis buski (caltrop and water chestnut corms)
Strongyloides stercoralis
Trichocephalus trichiuris
Intestinal myiasis-producing flies

On meats and sea-food:

Brucella abortus (pork?)
Salmonella aertrycke
Salmonella enteritidis
Salmonella suipestifer
Salmonella typhi-murium
Balantidium coli (pork)
Sarcocystis lindemani (pork, veal and beef)
Clonorchis sinensis (fish)
Dioctophyme renale (fish?)
Diphyllobothrium latum (fish)
Diphyllobothrium mansoni (fish)
Fasciola hepatica (sheep and goat liver)
Heterophyes heterophyes (fish)
Opisthorchis felineus (fish)
Opisthorchis viverrini (fish)
Paragonimus westermani (crab and crayfish)
Tænia saginata (beef)
Tænia solium (pork)
Trichinella spiralis (pork)
Intestinal myiasis-producing flies

CHAPTER XLII.

THE PROCESSES OF INVASION AND PATHOGENESIS.

True parasitism implies a living parasite on a living host. Each of the organisms concerned possess its full complement of life processes and it is only by the exercise of certain functions of its total vital activities that parasitism is possible. Unless the phenomena associated with the host-parasite relationship remain as integral parts of the vital activities of the contributing organisms the process is not parasitism, but intoxication.

The parasite and the host have evolved through change and adaptation and their evolution has progressed under such associations that each has been a factor in the environment of the other. Adaptation has permitted them to exist in each other's presence and in the case of the pathogenic parasite has allowed the parasite not only to live at the expense of its host but to do it harm.

Because no host-parasite relationship is permanent but is severed by the death of one or the other of the principals or their separation by other means, it is evident that the host and the parasite must possess functions by which they can renew their relationship with other partners. The assumption of this relationship by the use of certain vital processes on the part of each is termed *invasion*.

The invading parasite (which is also being "taken in" by the host) enters by way of particular host structures which up to this time have been in equilibrium. At the moment that a parasite which is genetically adapted to the host comes into contact with the particular host structures which it is able to invade a disequilibrium is created in the cells and tissues of the host. The processes of growth, metabolism, irritability and reproduction in the parasite affect the balances of the host and endanger them. That they do not necessarily disrupt them and produce irrevocable damage can only be due to a certain degree of tolerance possessed by the host cells to the specific character and amount of the forces tending to disturb them. Whether the parasite gains a firm foot-hold or is completely thwarted in its invasion, these earliest changes in the host must be the starting points in the development of disease from parasitic agents. In looking backward from the stage of the fully developed disease it is these earliest changes which must constitute the beginnings of pathogenesis. Malaria starts at the moment the sporozoites are liberated by the mosquito into the host tissues and not with the first clinical manifestations of the disease, nor even the

invasion of the first red cell by a sporozoite; typhoid fever has its onset with the entrance of the typhoid bacillus through the intestinal epithelium; hookworm disease commences with the boring of the infective larva through the skin.

In the foregoing discussion it has been assumed that the parasite has reached that portion or portions of the host anatomy that it is able to invade and in the preceeding section the parasites have been brought to the point of their first intimate relationship with the host. Between these two loci—the portal of entry and the point of invasion—lies a region full of hazards for the parasite and a zone of defense for the host. Among the bacteria and protozoa, few of the many which arrive at the portal of entry succeed in traversing the no-man's land of primary body defenses. The character of the surface coverings—skin and mucous membranes—and the nature of the mechanical and chemical processes of the channels by which organisms gain entry to the interior cavities of the body are such as to remove most parasites or destroy them before they can attach themselves to their favorite sites. Even though this defense may take place in an almost completely closed accessory nasal sinus or in the recesses of the small intestine it is still "outside" the tissues; there has been no invasion and no pathogenesis; no cellular equilibria of the host have been disturbed and no disease has so far resulted.

The large skin surface of the body must be constantly approached by myriads of pathogenic microörganisms and yet the variety and numbers of these pathogens which constitute the normal flora of the skin is surprisingly few. Mechanical removal by air, water and friction accounts for the failure of many bacteria to remain on the skin but it is becoming evident that there is some function of skin and its secretions which destroys in a relatively short time most of the organisms remaining on it. Arnold[1] and his co-workers have shown that the normal skin reduces the number of *Salmonella enteritidis* organisms placed experimentally on the skin of the palms so rapidly that none could be recovered after ten minutes. Those bacteria which constitute the normal flora—staphylococci and diphtheroids largely—cannot be entirely removed by the normal or any artificial processes of cleansing.

It is generally assumed that this cleansing property is due to the bactericidal action of perspiration although this is not proven. Fleming's *lysozyme*, a bacteriolytic substance found in many normal tissues and secretions, may account for some of the lytic activity of perspiration but Arnold and others incline toward the belief that most of the effect is due to the low pH of the normal skin (5.8–5.22).

The horny avascular layer of the skin is an effective mechanical

[1] Arnold, L., Gustafson, C. J., Montgomery, B. C., Hull, T. G., and Singer, C., Am. Jour. Hyg., 11, 345, 1930.

barrier which excludes organisms from the next susceptible layer of cells below it and its vascular channels.

Although fungi probably never form a part of the permanent flora of the skin, the pathogenic forms can gain a temporary habitat on the surface under favorable conditions of warmth and moisture. Dirt predisposes to their accumulation which is probably an index of a lack of their removal by mechanical means such as washing and the use of soap.

Among the protozoa, the leishmanias are temporary skin contaminants but unless the conditions for invasion are present at the time they probably do not persist on the external skin surfaces. The same is true of *Trypanosoma cruzi* in the feces of the bug which harbors it and contaminates the skin.

The skin penetrating larvæ of *Ancylostoma braziliense*, *Ancylostoma duodenale*, *Necator americanus*, *Loa loa*, *Onchocerca volvulus*, and *Wuchereria bancrofti* and the cercariæ of *Schistosoma mansoni* and *Schistosoma japonicum* cannot persist on normal skin unless they can very rapidly gain entrance to the deeper tissues.

The ova of *Enterobius vermicularis* can resist drying for a long period of time on the perianal skin but the larvæ do not penetrate through this route.

With the exception of *Phthirius inguinalis* and *Sarcoptes scabiei* no arthropod forms remain permanently on the surface of the skin. Their access to the skin is so nearly contemporary with their invasion that a discussion of their activities will be taken up under the latter heading. The eggs and larvæ of cutaneous myiasis-producing flies are present in dead tissue products or secretions on the skin and it is from these media that they invade the skin if at all.

The nose, mouth and pharynx are lined with relatively resistant cells which are normally impermeable to most bacteria. In addition, these surfaces are all moist with mucus or saliva which is in constant molecular movement across it or in actual strong fluid currents. The greater part of the mucous membrane cells of the nose also possess cilia which aid in the transportation of particulate matter and formation of fluid currents.

The posterior drainage of the nose and the suction and pressure forces between the tongue, gums, cheeks and palate combine to force bacteria-laden food and fluids backward to the pharynx from where they are removed by swallowing. As in the case of the skin only those few organisms which are well adapted to survive in the nose, mouth and throat can obtain a satisfactory lodging and multiply to form the normal flora of the mouth. Occasional pathogens can implant themselves on certain areas such as the faucial and pharyngeal tonsils and defects in the normal structures brought about by such conditions as hypertrophied turbinates, ill-drained

sinuses, carious teeth, hyperplastic or otherwise diseased tonsils, foreign bodies, malformations and injuries of many kinds.

The deeper recesses of the respiratory tract from the larynx to the alveoli of the lungs are also lined by moist secretions. A large part of the bronchial tree possesses ciliated epithelium which moves fluid-borne particles toward the exterior. This motion is probably aided by the aërodynamics of respiration and the respiratory movements of the lung and bronchial tissues themselves. Although there may be many varieties of organisms present in the bronchi at any moment, these organs are relatively sterile as regards permanent bacterial flora.

The fungi, *Blastomyces dermatitidis, Coccidiodes immitis, Torula histolytica* and *Actinomyces asteroides* can penetrate the deeper air passages as spores in the same way as bacteria and dust particles and are subject to the same mechanisms of expulsion. *Monilia albicans* can grow on the surface of the mucous membranes of the mouth and *Rhinosporidium seeberi* carried into the nose may take lodgment on the membranes.

No pathogenic protozoa or helminths enter through the respiratory tract, although the larvæ of *Ancylostoma, Necator* and *Ascaris* and the lung fluke *Parogonimus westermanni* may be found there after having entered by some other portal. Larvæ of *Strongyloides stercoralis* can invade from the mucous surfaces of the mouth.

There are no bronchial or pulmonary approaches for any of the arthropods but rhinal myiasis-producing flies may deposit their eggs and the larvæ on the mucous membranes of the nose. Under favorable conditions the larvæ may penetrate the accessory nasal sinuses and auditory canal.

The stomach and intestines bear the brunt of disposing of all organisms which gain entrance to the nose, throat, mouth and pulmonary areas and from which regions they are being continually removed and swallowed with saliva.

Few of the pathogenic bacteria survive passage through the acid juices of the stomach and duodenum in its normal concentration of hydrochloric acid. Those which resist the action of the acid are largely the very organisms whose special affinity is for the intestinal mucosa. It is probable that bulky foods and large volumes of fluid are able to protect bacteria in their passage through the acid-bearing regions. Once in the alkaline succus entericus the survivors are free to multiply and form the normal flora of the intestine. Abnormal processes of secretion and motility of the gastro-intestinal tract may so alter the acid-alkali relationship and the length of time to which bacteria are exposed to more or less favorable media that this defense may be weakened or strengthened against the alimentary pathogens. Researches of Goldsworthy and Florey,[1]

[1] Goldsworthy, N. E., and Florey, H.: Brit. Jour. Exp. Path., 11, 192, 1930.

and Arnold[1] on the rôle of lysozyme in the stomach and intestines have been inconclusive insofar as man is concerned.

Among the protozoa which enter by way of the gastro-intestinal tract the oöcyst of *Isospora belli* and *I. hominis*, cysts of *Balantidium coli*, and *Endamœba histolytica* and viable spores of *Sarcocystis lindemanni* are the only forms of these organisms able to survive passage through the acid stomach contents. Excystation of these protozoa takes place in the intestines before invasion.

None of the helminths are acquired through the alimentary tract in their adult stages. The following pathogenic worms can resist the action of gastric juice in the forms indicated and are frequently incorporated in solid animal foods: as ova—*Ascaris lumbricoides*, *Dioctophyme renale*, *Echinococcus granulosis*, *Enterobius vermicularis*, *Hymenolepis nana* and *Trichocephalus trichiuris;* as cysts—*Clonorchis sinensis*, *Opisthorchis felineus*, *Opisthorchis viverrini* and *Paragonimus westermanni;* as a sparganum— *Diphyllobothrium latum* and possibly *Diphyllobothrium mansoni;* as cercariæ—*Fasciola hepatica*, *Fasciolopsis buski* and *Schistosoma hematobium;* as cysticerci—*Tænia saginata*, and *Tænia solium;* as larvæ—*Dracunculus medinensis*, *Heterophyes heterophyes*, *Strongyloides stercoralis* and *Trichinella spiralis*.

The spores of *Monilia albicans* are the only forms of pathogenic fungi which can enter the intestines of man by way of the alimentary tract.

The larvæ of the intestinal myiasis-producing flies survive passage through gastric juice. The only other representative of the arthropods which enters by the alimentary canal is *Porocephalus armillatus* which does so in egg form in water.

The mucous membranes of the urinary channels can be considered sterile although they offer portals of entry for some pathogenic bacteria especially *Neisseria gonorrhœæ*, *Treponema pallidum* and various forms of streptococci, staphylococci and *Escherichia coli*. The vagina of the female normally contains no pathogenic microörganisms but is susceptible to those listed under the urinary tract and *Corynebacterium diphtheriæ* in addition.

When a parasite has been brought to the tissue of the human host which it can invade and finds there a suitable medium in which it can survive and undergo necessary changes in its life-cycle or multiply and produce a colony, it is free to exercise its vital activities in the direction of invasion. Although there are similarities in the processes employed by the various classes of parasitic organisms the differences are so marked as to make it necessary to consider them in groups.

Bacteria.—*Bacillus anthracis.*—Invasion by inoculation through breaches in the skin. No exotoxin known. Slight evidence of an

[1] Arnold, L.: Am. Jour. Hyg., 8, 601, 1928.

endotoxin in extracts from broken-up organisms. Bail believes that aggressins play the major rôle in assisting in the multiplication of the bacteria and interference with the protective actions of the body. Capsule formation is correlated with virulence. Little is known of the causes of pathogenesis further than the local effects. Mechanical capillary obstruction may be an important factor. Moderately antigenic exotoxin: agglutinins, precipitins and alexin-fixing substances.

Bartonella bacilliformis.—Passive invasion through the bite of Phlebotomus which transmits it.

Brucella abortus.

Brucella melitensis.—Invasion of epithelial cells of intestinal mucosa (milk-borne type)—passive inoculation through skin abrasions or possibly by the bites of blood-sucking insects. Rapid spread throughout the body from the minor local lesion. No exotoxin production. Moderately antigenic:—agglutinins. Slightly sensitizing.

Clostridium histolyticum.

Clostridium novyi.

Clostridium œdematis-maligni.

Clostridium welchii.

Spores of anaërobic saprophytes in damaged host tissue to which they have gained access by contact or inoculation. Germination of spores to vegetative forms. Liberation of powerful histolytic exotoxins. Multiplication and spread of organisms in newly-damaged tissue. Antigenic: agglutinins, precipitins. Antitoxigenic.

Clostridium tetani.—Passive introduction of spores through inoculation or contact with devitalized tissues. Germination and institution of metabolic activities with liberation of a powerful neurotropic exotoxin which acts on nerve tissues far removed from the seat of infection, and a second exotoxin destructive to red cells and leukocytes. The organisms do not histolyze tissue cells and rarely spread from their point of invasion. Latent spores in tissues may be activated by trauma and chemical changes in the tissues which debilitate the cells among which the clostridia are living. Tetanus neonatorum occurs from contact infection of the umbilical cord. Strongly antigenic. Weakly antitoxigenic in natural infections in man.

Corynebacterium diphtheriæ.—Vegetative forms in contact with susceptible mucous membrane cells elaborate histolytic toxins which destroy cells and produce a coagulated fibrinous exudative reaction. Minimal extension of organisms beyond the pseudomembrane. Liberation of a powerful soluble neurotropic exotoxin. Possibly a phagocytosis-inhibiting endotoxin. Moderately antitoxigenic in natural infections in man. Sensitizing.

Diplococcus pneumoniæ.—Organisms on contact with susceptible broncho-pulmonary epithelium penetrate through some unexplained mechanism and spread through the supporting tissues. No definitely conclusive evidence of locally acting tissue toxins. Substances of the organism sensitize the tissues and the resulting allergic tissue phenomena largely characterize the disease. The organisms readily gain access to lymph and blood channels and produce septicemia. Type—specific polysaccharide in capsule (aggresin?). Antigenic: Species specific nucleoprotein. Soluble exotoxin.

Eberthella typhi.—Multiplication of organisms in the small intestine. Entrance through the mucosa into the lymphatics, Peyer's patches and agminated lymph follicles and eventually into the blood stream. No positive identification of an exotoxin or endotoxin responsible for the symptomatology of the disease has been made. Antigenic:—agglutinins (H and O). Alexin-fixing. Sensitizing locally.

Escherichia coli.—Invades the intestinal epithelium under some unknown influences which make this normal inhabitant of the intestinal canal become pathogenic. May enter through lesions produced by other disease processes and may be carried through by phagocytes during certain stages of digestion. Liberates an endotoxin on disintegration. Not antitoxigenic. Antigenic: bacteriolysins, agglutinins, precipitins.

Fusiformis fusiformis.—Knowledge of the rôle of this organism in Vincent's angina and its constant association with a spirochete is at present in such a state of confusion as to preclude any specific statements relative to its mode of invasion or pathogenesis.

Hemophilus ducreyi.—Probably invades only by way of broken skin. Sensitizing.

Hemophilus influenzæ.—Probably enters directly through the epithelium of the respiratory tract and produces inflammation. Its entry may be augmented by concurrent effects of other organisms or a virus. Very slightly agglutinogenic. Causes some increase in opsonins in the first week of influenza.

Hemophilus pertussis.—Nothing is known of the mechanisms of invasion. Antigenic:—agglutinins (4 antigenic groups—Phase I, II, III, IV corresponding to growth characteristics). Exotoxin and endotoxin-forming. Alexin fixation.

Klebsiella granulomatis.—Probably a secondary invader in a skin lesion produced by some other organism.

Klebsiella pneumoniæ (Friedländer).—Toxic products possess a direct specific affinity (Zinsser) for lung cells. Antigenic:—soluble specific capsular substance when attached to somatic protein stimulates production of type specific antibodies—precipitins and agglutinins.

Loefflerella mallei.—Introduced passively into a wound or scratch in the skin and produces histolysis and suppuration. Generalized dissemination. Strongly sensitizing to the whole body. Antigenic: agglutinins. Alexin-fixing.

Mycobacterium lepræ.—Location and mechanism of invasion not known. Earliest changes of pathogenesis not known. Sensitizes. No antigenic properties demonstrable.

Mycobacterium tuberculosis hominis.—Invasion through skin abrasion (passive introduction); tubercle bacilli can pass through the intestinal mucous membrane during the first ten days of life without producing any lesion in the intestinal wall (Gay); invasion through the mucosa of the mouth; invasion from the epithelium of the respiratory tract by phagocytized cells which carry it into the tissues. Secondary dissemination by lymph stream. Ingestion of bacilli by macrophages, degeneration of the parasitized cells.

Tubercle-lipoid (Phosphatid A3).—Causes local stimulation and accumulation of monocytes which eventually form the epithelioid cells. Phthioic acid from Phosphatid A3 produces the same reactions. Antigenic: alexin-fixing. Non-sensitizing.

Polysaccharides.—Cause migration and destruction of leukocytes. Non-antigenic. None-sensitizing.

Proteins.—Call forth plasma cells. Actively antigenic. Highly sensitizing.

Mycobacterium tuberculosis bovis.—Invade man almost entirely in early life through the buccal and intestinal mucosa.

Mechanisms of pathogenesis similar to those of the human variety with only slight type-specific differences in the reactions.

Neisseria gonorrheæ.—Cellular invasion of the mucous membranes by the cocci. Liberation of toxins with production of inflammation. Loosening of epithelial cells and sloughing.

Endotoxin and exotoxin formed (gonotoxins). Protein-free type-specific substances probably produce allergy. Carbohydrate-free protein substances produce non-specific reactions.

Neisseria intracellularis (meningitidis).—Micrococci on the pharyngeal mucoa set up a mild rhinopharyngitis which is believed in some way to weaken the normal barriers against the organism. Extension from the submucous tissues to the brain is most probably by way of the blood stream although some still hold to direct extension by lymphatics or through the walls of the sphenoid and ethmoid sinuses.

Produces a powerful endotoxin which is liberated when the organisms are destroyed by lysis. Exotoxin?

Antigenic: type-specific precipitins.

Pasteurella pestis.—Organism passively introduced through the skin by the bite of the transmitting rodent flea; implanted on the respiratory mucosa, it in some unknown way enters the lym-

phatics, is carried to a bronchial lymph node and secondarily invades the lung.

Produces no soluble toxin. May liberate some endotoxin-like substance which is agglutinogenic.

Pasteurella tularensis.—Organism passively introduced through the skin by the bite of the transmitting arthropod or from infective material through a skin abrasion; invasion by necrosis of the cells of the respiratory mucous membrane. Dissemination to regional lymph nodes producing there a toxic necrosis. Antigenic: agglutinins.

Salmonella aërtrycke.
Salmonella enteritidis.
Salmonella paratyphi (Paratyphoid A).
Salmonella suipestifer.
Salmonella schottmülleri (Paratyphoid B).

Organisms and their toxic products in the intestinal canal exert an intense direct toxic effect on the mucosa. In the paratyphoid groups organisms gain entrance to the submucosa and produce a generalized disease.

The entire group possesses a common somatic agglutinogenic antigen. Type-specific agglutinogens are produced by each organism. Toxic growth products are present in the food in which they have been introduced. They are therefore responsible for their particular types of food poisoning.

Shigella dysenteriæ var. *Flexner;* var. *Shiga-Kruse;* var. *Sonne* (Duval).—Direct action of bacterial toxins on cells lining the intestinal mucosa producing degeneration and necrosis. Organisms remain localized in submucous tissues but few may be carried to the mesenteric lymph nodes. Toxins absorbed and affect distant organs particularly the central nervous system (var. *Shiga*).

Exotoxin from var. *Shiga*. Endotoxins produced by *Shiga* and *Flexner.*

Antigenic: agglutinins, bacteriolysins, precipitins. Alexinfixation.

Staphylococcus albus.
Staphylococcus aureus.
Staphylococcus epidermidis.

Passive introduction through the skin by way of abrasions, cuts and penetrating instruments; passive introduction into hair follicles and sebaceous gland ducts by mechanical forces such as rubbing, obliteration of the mouths of the ducts by dirt, inspissated sebum; implantation on susceptible mucous membranes and internal organs (uterus, bladder, urethra); multiplication in these sites under favorable abnormal conditions Phagocytosis by polymorphonuclear cells which are destroyed by the process. Toxic products (necrotoxins) of the organisms and degenerated and destroyed tissues cause still further destruction and the formation of pus.

Antigenic exotoxin: agglutinin, hemolysin, leucocidin.
Streptococcus epidemicus.
Streptococcus erysipelatos.
Streptococcus hemolyticus (pyogenes).
Streptococcus scarlatina.
Streptococcus viridans.

Passive introduction through the skin by way of abrasions, cuts, penetrating instruments, multiplication in pockets in hair follicles, sebaceous gland ducts, gingival folds, tonsillar crypts, genital tract glands; abnormal tissues affected by pre-existing disease due to other organisms or inanimate agents.

Toxic enzymes produced by the cocci probably affect the cells in their immediate neighborhood and cause histolysis. Polymorphonuclear leukocytes phagocytize the organisms and may be destroyed in the process by leucocidins.

Antigenic: hemolysin production is an outstanding but type-variable specific characteristic. Organisms possess a type-specific antigenic protein, species specific non-antigenic carbohydrate and a group or species specific antigenic nucleo-protein. Agglutinins, opsonin.

Soluble exotoxin: antitoxigenic capacity varies with the types. Sensitizing powers vary with the types.

Vibrio choleræ.—Primary toxic irritation of intestinal epithelial cells. Invasion of cells by vibrios in tissue and intestinal contents. Powerful "endotoxins?" exotoxins?

Antigenic powers: agglutinins, precipitins. Anti-toxigenic. Non-group specific agglutinating carbohydrate fraction. Flagellar and somatic antigens.

Filterable Viruses with Inclusions.—**Group I.**—*Foot and Mouth Disease Virus.*—Virus in contact with skin cells invades them and produces degenerative changes. Accompanied by cell inclusions. Weakly antigenic of short duration.

Herpes Simplex Virus.—The virus invades skin cells apparently when some factors such as trauma, cold and heat, and febrile disease lower the local resistance. The virus enters the nuclear material of the cells and causes chromatic changes and degeneration. Accompanied by cell inclusions. Antigenic, producing antivirucidal substances.

Molluscum Contagiosum Virus.—Invasion of the living skin cells with subsequent stimulating effects on the cells which produce a neoplastic growth. Inclusion bodies found only in the cytoplasm.

No evidence of antigenic powers.

Psittacosis Virus.—Virus in contact with respiratory epithelium causes hypertrophy and hyperplasia of the alveolar cells. Inclusion bodies found in the mononuclear cells.

Probably strongly and permanently antigenic with the production of neutralizing antibodies.

Rabies Virus.—Inoculation through a breach in the skin or mucous membranes permits the virus to approach the cells of the central nervous system which it invades. Negri bodies formed within the cells and contain small refractile inclusion bodies. Virus produces degenerative changes in the invaded cells. Strongly antigenic; neutralizing antibodies. Alexin-fixing.

Rift Valley Fever Virus.—Accidental inoculation of virus through the skin permitting invasion from the blood stream of parenchymatous cells particularly of the liver. Necrotic degeneration of invaded cells. Inclusion bodies in the nuclei of cells.

Antigenic: neutralizing antibodies. Alexin-fixing.

Vaccinia virus.

Variola virus.

Entering probably through the respiratory mucosa, the virus is brought in contact with epithelial cells (dermotropism) invades them and becomes surrounded by a plastin substance manufactured by the cell (Gay.) Growth of the Guarnieri inclusion bodies until they break up into elementary bodies and are liberated on the destruction of the host cell.

Strongly antigenic: neutralizing antibodies.

Verruca Vulgaris Virus—Inoculation through a wound brings the virus in contact with the growing skin cells which it invades and stimulates to form neoplastic growth. Intranuclear inclusion bodies.

Yellow Fever Virus.—Inoculation into the blood stream by the specific virus-carrying mosquito (*Aëdes*). Dissemination throughout the body with selective invasion of the parenchymatous organ cells. Degeneration of capillary epithelium and hepatic and renal cells especially. Intranuclear inclusion bodies.

Strongly antigenic, producing permanent neutralizing antibodies.

Group II.—*Varicella Virus.*—Entering probably through the respiratory mucosa, the virus invades the rete cells of the skin and causes their degeneration and liquefaction. Inclusion bodies found only in testicular cells of monkeys inoculated with material from human skin lesions.

Antigenic: produces permanent virucidal substances.

Group III.—*Herpes Zoster Virus.*—Route of invasion of the body is unknown but the virus apparently enters the epithelial cells and produces a "ballooning degeneration" (Unna). No knowledge as to its immunologic powers.

Filterable Agents Without Inclusions.—*Common Cold Virus.*—The specific virus appears to attack the epithelial cells lining the nose and upper respiratory tract and is present in the cell-free exudate. It has not been demonstrated within any tissue cells. The presence

of other microörganisms in the nose seems to prepare the cells for the action of the virus. Other agents such as cold, chemicals, mechanical irritants and foreign proteins may act in a similar manner.

Smiley produces epidemiological evidence that the virus produces immune bodies of short duration.

Dengue Fever Virus.—The virus is passively inoculated into the blood by the virus-bearing mosquitoes (*Aëdes* largely). It has never been recovered from any tissue cells so that nothing is known of its mechanisms of pathogenesis.

Epidemiologic and clinical evidence indicates that it produces some relatively lasting immune antibodies.

Alexin-fixation has been reported.

Mumps Virus.—Nothing is known of the methods of invasion or early processes of pathogenesis of this disease other than the fact that the virus is present in mouth washings and inflammatory reactions occur in the salivary glands and ducts and secondarily in the testicles.

It is apparently strongly immunizing for an attack produces lasting immunity.

Pappataci Fever Virus.—Virus inoculated into the tissues through the bite of the sandfly and gains admission to the blood stream from which it can be recovered.

No certain evidence of its immunizing powers.

Poliomyelitis Virus.—Entrance of the virus into the central nervous system is presumed to occur by way of the naso-pharyngeal mucosa but this is not proven and rests largely on finding the virus in naso-pharyngeal washings. Within the central nervous system it is propagated along the axis cylinders and produces an acute inflammatory degeneration of the spinal and cerebral ganglia cells and those of the anterior horn of the spinal cord.

Strongly antigenic, producing lasting virucidal and neutralizing substances.

Presumably Filterable Viruses.—*Epidemic Encephalitis.*—Strong experimental evidence from transmission of infective material from the nasal secretions of human cases to rabbits. Some believe that it is a neurotropic strain of herpes virus operative under peculiar conditions of susceptibility on the part of the host (Gay, McKinley). Apparently an invasion of the ganglia cells in the pons and basal ganglia.

No direct information on the production of immune bodies is at hand but epidemiologic evidence points toward widespread resistance.

Epidemic Influenza.—Evidence for a transmissible virus rests on transmission experiments using nasal washings from human cases. Invasion is probably directly through the cells of the res-

piratory epithelium. It produces a pneumonic or catarrhal inflammation of the involved tissues.

Immune substances are probably produced but last only a short while.

German Measles.—Nothing known about the modes of invasion of the causative organism which itself remains undemonstrated. Produces lasting immunity.

Measles.—If due to a filterable virus, invasion probably takes place through some part of the respiratory tract epithelium. A filterable agent has been recovered from the blood and naso-pharyngeal secretions of measles cases which is able to produce the disease in monkeys. Pathogenesis so far as known is inflammatory in nature, catarrhal in the mucous membranes and perivascular infiltration in the skin lesions.

Antibodies are produced and are to be found in convalescent serum.

Rickettsias.—*Dermacentroxenus rickettsiæ.*—Passively introduced into the tissues of the host through the bite of an infected tick. Disseminated by the blood stream, it invades the endothelial cells of the small blood-vessels in the skin, subcutaneous tissues and testicles producing a proliferating endarteritis.

Spirochetes.—*Borrelia minus.*—Passively introduced through the skin of the host by way of a scratch or bite by the infected animal. Slow multiplication of organisms at site of wound. Later dissemination by the lymph stream and active motile invasion of the regional lymph nodes. Antigenic: lysins. Alexin-fixing.

Borrelia recurrentis.—Passively introduced into the host through abrasions of the skin produced by scratching where there is infected louse or tick feces or the crushed bodies of these infected arthropod hosts.

The organisms enter the blood stream and multiply freely at intervals of one or two weeks. It does not invade cells.

Antigenic powers: Agglutinins, lysins (type specific). An attack generally confers lasting immunity.

Leptospira hebdomadis.—The active leptospira on the urine-contaminated skin enter by way of any minute abrasions which may be present and actively gain admission to the blood stream where multiplication can take place. It does not invade cells.

Antigenic powers: Lysins, agglutinins.

An attack generally confers lasting immunity.

Leptospira ictero-hæmorrhagica.—Leptospira work their way out of the urine or infected water on the skin into the openings of small abrasions and enter the deeper tissues and blood stream. Multiplication takes place in the blood in the small interstitial blood-vessels of the viscera. Inada believes that the organisms can gain entrance by active penetration of the alimentary mucosa.

They do not invade cells.

Antigenic powers: Lysins, agglutinins and "agglomerating" antibodies. Alexin-fixing.

An attack confers lasting immunity.

Treponema pallidum.—Active penetration through intact skin or mucous membranes to the deeper tissues, or entrance through a wound. Dissemination through the lymph channels and blood stream. Selective affinity for the medial layers of arteries where they multiply. Toxic degeneration of fixed tissue cells and mobilization of mononuclear leukocytes. Dermotropic and neurotropic strains are believed to exist although the nature of the tropism has not been determined.

Antigenic powers: There are no demonstrable immune bodies in syphilitics although clinical evidence indicates some degree of immunity whether it be "infection immunity" or refractoriness to invasion during active infection or tissue immunity.

Strongly alexin-fixing. Non-sensitizing.

Treponema pertenuis.—Inoculation by rubbing into some breach in the skin such as a scratch mark, insect bite, or previous skin lesion. Local histolysis and low grade proliferative reaction. Dissemination by lymph channels to lymph nodes, and by blood stream to distant tissues. Toxic necrosis in secondary and tertiary lesions.

There is no evidence of the development of humoral immunity. Relatively permanent immunity after recovery. Alexin-fixing.

Treponema vincenti.—Believed to be invasive only in areas lowered in resistance by previous disease or traumatism. Causes necrosis in the presence of *Fusiformis fusiformis* and possibly other necessary accompanying organisms.

Nothing is known of its immunologic powers.

Fungi.—The pathogenic fungi appear to possess little invasive powers on normal tissues and in most instances there is indication that there has been some antecedent injury.

On the skin, the *epidermophytons* having found a suitable media for growth, begin to invade the horny layer in areas where it has become softened and macerated by a combination of heat, moisture and friction. Slight abrasions may also serve as a point of invasion into the horny layer. Invasion takes place by the insinuation of mycelial threads between and into the cells of this region. There is separation of the outer layers resulting largely from mechanical displacement but probably also by some chemical action of growth products. Specific agglutinins are formed against it. They elicit allergic response.

The *endodermophytons* invade in a similar way but in addition may be passively introduced by penetrating inoculation. The mycelial threads and mycelial spores invade the cleavage spaces between the rete layer and the granular layers. This is accompanied

by a non-specific inflammatory reaction beneath it. Secondary infection by bacterial organisms accounts for much of the severe manifestations. Specific agglutinins are formed against it. They elicit allergic response.

The *trichophytons* invade the hair follicles and the tissues around them by sending out mycelial threads which spread on the surface of the hair (ectothrix) or in the hair (endothrix). They can also invade the nails. Damaged epithelial cells desquamate and the infected hairs fall out. Inflammatory reactions appear around the hair bulbs and there may be pus formation. Dissemination by lymphatics to regional lymph nodes is not uncommon and blood-stream infection may occur with secondary skin lesions. Produces sensitization to a toxic trichophytin.

The *achorions* invade the hair and the tissues about its base. In this latter location it forms a dirty yellow sheath (scutela) around the proximal part of the hair. The hairs become lifeless and brittle and break off just above the sheath.

Microspora invade the bulb region of the hairs and form a sheath of small round cells or so-called spores about it. The hairs become brittle and break off.

Hormodendron (spp.) is one of the most superficial-growing of all of the skin fungi. Much of its growth is in the outermost horny layers with which it is constantly being thrown off in branny squames. The skin beneath the involved area is subject to depigmentation probably due to interference with the absorption of ultra-violet radiations of sunlight.

Torula histolytica (*cryptococcus*).—These budding organisms, present on the skin, or in the mouth, naso-pharynx or intestines invade these tissues in some unknown manner without leaving any obvious lesions. Dissemination is probably through the blood stream to bone, subcutaneous tissues, lung, or meninges and brain. In these regions they call forth a pseudogummatous response with destruction of tissues and stimulation of some cells to form a myxomatous, sarcoma-like tumor.

Produces allergic sensitization and is alexin-fixing.

Blastomyces dermatitidis is introduced into the skin by direct inoculation, probably most frequently by vegetable spicules such as thorns, splinters, straw, etc. Germination of the spores takes place with the formation of mycelia. Invasion by way of the lung is probable but its mechanism is unknown. Entry through this way may result in systemic dissemination. The tissue reaction to the growing and extending fungus is papillomatous in structure with small abscess formations.

Does not produce allergy or alexin-fixing substances.

Monilia albicans on the skin or mucous membranes of the mouth appears to invade only when there is some other condition present

which alters the resistance of the cells,—malnutrition, tuberculosis, diabetes, prolonged moistness of skin surfaces, and in the intestines disturbances of the secretory functions of the stomach, intestines and pancreas. The organism grows superficially in the horny layers of the skin and nails and in the superficial mucosa. Occasionally gangrene or noma of the mouth may occur but this may not be entirely due to the fungus.

It produces specific agglutinins and skin sensitization. Cutaneous sterile lesions called levurides or moniliids occur as a result of allergic reactions.

Coccidioides immitis appears to invade either through the skin or pulmonary epithelium although nothing definite can be stated as to the mechanisms involved. Extension to the lymphatics and systemic dissemination follows from either source of invasion. Subsequent pathogenesis is nodule and abscess formation in the skin and subcutaneous tissues, bones, joints, lung, brain, cord and all viscera except the gastro-intestinal tract.

It produces precipitin and agglutinin response, is alexin-fixing and sensitizing.

Sporotrichum, spp. are generally introduced by direct inoculation through the skin, most frequently on the back of the forearm. Occasionally generalized and secondary local lesions result from invasion from some hidden focus. Multiplication and extension of the fungus takes place in the subcutaneous spaces and lymph channels although the regional nodes are seldom involved. The reaction is granulomatous in nature.

It produces agglutinin response, is alexin-fixing and produces cutaneous sensitization.

Madurella mycetoma is probably always introduced through the skin by inoculation from some injury such as sharp grasses, splinters, stones, etc. Multiplication occurs in the deep subcutaneous tissues with granulation tissue formation, abscess, and arteritis. Many of the subsequent changes are probably due to defective blood supply in parts dependent on the arteries involved. The granules of Madura foot are colonies of fungi.

Actinomyces bovis when present in the mouth can probably only invade the mucous membrane when there is some injury such as that produced by extraction of a tooth, laceration by plates, jagged teeth, or traumatism by any foreign body.

The ray fungus introduced into the submucosa causes an inflammatory reaction with nodule formation and suppuration. Conglomeration of nodules forms tumor-like masses which break down and cause cavities and fistulæ.

Dissemination can be by direct extension, by the lymphatics, or by erosion into a blood-vessel and spread by the blood stream.

Primary invasion may occur through the lungs, rarely through the intestinal mucosa, or through the skin.

Agglutinins present during the height of the disease.

Actinomyces maduræ is introduced into the subcutaneous tissues by inoculation, generally by objects penetrating the bare foot. A granulomatous reaction is produced at the site of multiplication of the fungus with suppuration and sinus formation. The disease remains localized.

Protozoa.—The pathogenic protozoa depend in large part on their motile powers to invade cellular spaces and to penetrate cell membranes of the host cells which they parasitize. That they also utilize some chemical products of their own or the results of their activity against the cells among or in which they grow is evidenced by the presence of agglutinating antibodies in the host serum and presumably by the appearance and changes in the invaded tissues. In this class of organisms the growth and multiplication processes are so clear cut that they present outstanding evidence that their own vital activities are solely responsible for the host reactions which constitute the disease.

Balantidium coli.—The vegetative, actively motile form, living free in the large intestine, appears to be positively attracted by the epithelial cells. Under observation, the balantidium has been seen to bore its way between cells by a rotating motion activated by the cilia and it is assumed that this mechanical displacement of cells is operative in the actual conditions in the intestine. The necrotic appearance of the cells in balantidial ulcers suggests the action of a proteolytic enzyme although this has not been proven. Once in the subepithelial tissues the parasites undergo rapid subdivision and form nests which are characteristic of the disease. It is not known how far secondary invasion by bacteria is responsible for the complete picture.

Endamœba histolytica.—Whether or not the pathogenic ameba is assisted in its invasion by the use of cytolytic enzymes, it remains fairly certain that the active movement by pseudopodia dominates the picture of penetration and extension of amebæ in the mucosa of the intestine. Craig[1] believes that he has demonstrated the presence of a cytolytic factor but Ratcliffe[2] explains pathogenesis as being due to the mechanical opening up of the lymph channels by the ameba and the entrance of bacteria through these artificial atria. Hiyeda and Suzuki[3] support Craig's contention that cytolysis is an important factor. The results of tissue necrosis and the accumulation of the products of host reaction still further interfere with the nutrition of undermined mucosa and undoubtedly contribute to the extent of the lesion on the surface of the mucosa.

[1] Craig, C. F., Am. Jour. Trop. Med., 7, 225, 1927.
[2] Ratcliffe, H. L., Am. Jour. Hyg., 14, 337, 1931.
[3] Hiyeda, K., and Suzuki, M., Am. Jour. Hyg., 15, 809, 1932.

Clinical evidence makes it highly presumptive that the host reacts to produce antibodies of some as yet undetermined nature which account in part for the apparent differences in resistance of individuals to infection, but other factors, such as diet (carbohydrate, proteins, liver extract) may be of equal or more importance.

Craig has demonstrated the presence of alexin-fixing substances.

Isospora belli.

Isospora hominis.

The active sporozoites liberated from the oöcyst in the intestine actively invade the epithelial cells of the mucosa by direct penetration through the cell membrane. The processes of schizogony and liberation of the merozoites is destructive to the host cells and if the number of infected cells is great enough will result in clinical coccidiosis.

Leishmania donovani.—The non-flagellated forms of the parasite are probably inoculated directly into the tissues of the host through the bite of the sandfly *Phlebotomus chinensis*. From the area where they are deposited they are taken up by the macrophages of the reticulo-endothelial system. Multiplication and subsequent parasitism of more cells results in a massive and extensive increase in the reticulo-endothelial elements which is the characteristic pathology of Kala-azar. Herpetomonad flagellate forms rarely if ever occur in man.

No antibodies have been demonstrated in man as a result of these processes.

Leishmania braziliensis.

Leishmania tropica.

The non-flagellated forms of these two parasites gain admission from the surface of the body through pre-existing skin lesions (contact inoculation) and possibly through the bite of a sandfly which is suspected although not proven to be a carrier.

From the site of inoculation they are engulfed by macrophages. Their multiplication is largely confined to the neighborhood of the area of inoculation and results in ulceration. The ulcer due to *L. tropica* is called Oriental Sore, and that caused by *L. braziliensis*, Espundia, Uta or Forest Yaw.

An attack of Oriental Sore produces immunity but no such protection has been demonstrated in Espundia.

Plasmodium falciparum.

Plasmodium malariæ.

Plasmodium vivax.

The malaria-producing parasites are all introduced into the blood of the human host by direct inoculation through the action of the mosquito as it obtains a blood meal. The free-living sporozoites are liberated into the blood stream and soon after, penetrate the

erythrocytes by their own active movements. The metabolic processes of the organisms inside of the red cells are completely devastating to the function and structure of the host cells. They are actively ameboid in the cytoplasm of the red cell and exist at the expense of the nutritive elements they find there. As they multiply and form the rosettes of merozoites the red cell loses its normal pigment and enlarges to accommodate the increased amount of parasitized matter. The hemoglobin is metabolized to hemozoin.

With the maturation of the merozoites the red cell bursts and liberates the new parasites which are freed and enabled to parasitize new erythrocytes.

The clinical manifestations of chill and fever coincide with the liberation of merozoites and are probably due to a toxin produced by the parasites or the damaged erythrocytes, although the existence of the first has not been identified or proven.

Although it is readily demonstrated by studies on endemicity of malaria that individuals differ in their susceptibility or resistance to infection with malaria parasites there is no evidence that this is due to any permanent antibody immunity. At this writing the consensus of opinion is in favor of the resistance being of the type seen in latent infection which is prohibitory to superinfection, or that repeated new infections keep down the clinical manifestations of active malaria by some other mechanism.

Trypanosoma cruzi.—While it has been demonstrated that the bug *Panstrongylus megistus* is the vector of this trypanosome it has been shown that the leishmania form of the parasite is not inoculated through the bite of the bug, but that infected feces of megistus deposited on the skin at the time of the bite is rubbed into the lesion. The parasites are taken into tissue cells where they multiply and become transformed into crithidia at the expense of the cell.

When the invaded cell bursts the liberated trypanosomes invade other cells in the organs to which they have been distributed.

Nothing is known of any immune reactions resulting from this parasite.

Trypanosoma gambiense.

Trypanosoma rhodesiense.

The metacyclic phases of these parasites are carried out of the salivary ducts of the tsetse-fly in the act of biting and injected directly in the skin of the host. They multiply free in the blood stream by fission and have a tendency to accumulate in the lymph nodes which are characteristically enlarged. Invasion of heart muscle cells and neurologia cells of the central nervous system are reported and trypanosomes have been found in the spinal fluid. It is assumed that a toxin is produced at some time during the life cycle in the human but this fact has not been definitely established.

The reported agglutinating and agglomerating powers of human serum from active cases lack confirmation although it is agreed that there may be some such natural resisting mechanism against *T. gambiense.* There is no such resistance to *T. rhodesiense.*

Helminths.—Because the helminths are metazoan parasites and have differentiated parts which perform particular functions there is necessarily a wide range in the mechanisms that they utilize for invasion and production of disease.

Ancylostoma braziliense.—The infective filariform larva actively bores its way into the hair follicles, penetrates the living cells and invades the Malpighian layer of the skin. In this position it calls forth, apparently through the action of toxic body products, a mononuclear leukocyte reaction with the accumulation of eosinophiles. The parasite burrows along the *stratum malpighii* just beneath the granular layer, making a channel wherever it goes. The channel shows inflammatory response with vesicle formation and sometimes acute bacterial inflammation due to secondary invaders.

Ancylostoma duodenale.

Necator americanus.

The infective filariform larvæ which have lost their sheath in the soil or shed them at the time of invasion through the skin, insinuate their head ends into the hair follicles and then penetrate the cells lining the follicle and invade the subcutaneous tissue. At this point they set up a toxic, irritative inflammatory reaction known as "ground-itch." Secondary invasion by bacteria at this stage may produce suppuration. The active larvæ crawl along the lymph spaces and are either caught up by the lymph stream and carried to the regional lymph nodes, or they enter blood capillaries and are swept on to the right heart and into the pulmonary circulation. In the lungs the larvæ reach the alveolar capillaries, pass through their walls and between the cells of the alveolar epithelium and make their exit into the air spaces. From here they migrate into the bronchioles and bronchi where they are propelled forward by the mucus, ciliated epithelium, expiratory mechanisms and their own movements into the trachea and larynx. On reaching the epiglottis and pharynx they are caught up in the stream of materials swallowed from the mouth and are carried by way of the esophagus, stomach and duodenum to the upper parts of the small intestine where they attach themselves to the mucous membrane. At this point they undergo further development to the adult stage.

In their passage through the lung tissues they produce mechanical injury to the capillary vessels with subsequent hemorrhage and probably exert some toxic or irritative effect on the epithelium.

The adults in the intestine deplete the host of blood and probably

secrete some body principle which is strongly inhibitory to hematopoiesis.

Ascaris lumbricoides.—The newly hatched larvæ in the small intestine actively bore their way through the intestinal epithelium and invade the submucous lymph spaces. From here they attain the right side of the heart either by direct invasion of the portal radicles and mesenteric veins or by the lymph channels and thoracic duct. From the right heart they are swept into the capillaries of the pulmonary circulation. They bore their way out of the capillaries and through the alveolar epithelium into the air spaces. In so doing they produce hemorrhages and toxic inflammatory reactions. They continue to grow during a brief stay in the smaller air passages and then migrate or are carried by secretions into the bronchi, trachea and larynx, successively. In their emergence through the glottis into the pharynx they are caught in the mechanisms of swallowing and carried to the stomach. Here, they resist the acid secretions and are projected on with the stomach contents into the small intestine. Without attaching themselves they grow freely in the intestinal contents and reach adulthood.

Migrating larvæ may accidentally invade systemic capillaries and be carried to distant organs where they set up severe inflammatory reactions.

Adults in the intestinal lumen secrete an as yet unidentified toxic material which in susceptible individuals produces allergic reactions.

They cause disease by nerve reflex irritations and mechanical blocking of the intestinal tract itself or of its accessory channels such as the vermiform appendix, diverticulæ, or the bile ducts.

Clonorchis sinensis.—Excysted adolescariæ attach themselves immediately to the duodenal mucosa and by some attraction work their way along the mucosa to the opening of the common bile duct. They then actively migrate up the bile ducts to the biliary radicles in the liver where they stop wandering and develop into adult flukes.

Faust[1] has shown that the flukes produce a proliferative reaction with cyst formation and multiple production of new biliary capillaries. He finds no direct evidence of general toxicosis but attributes liver lesions in the neighborhood of the worms to some toxic secretion.

Dioctophyme renale.—The matured larva, freed from the ingested cyst in the stomach or intestine finds its way by some unknown route to the pelvis of the kidney where it grows to adult size. Nothing further is known of its pathogenesis other than as it acts as an obstruction in the urinary tract and by gradually destroying the renal parenchyma.

Diphyllobothrium latum.

Diphyllobothrium mansoni.

[1] Faust, E. C: Human Helminthology, Philadelphia, Lea & Febiger, 1929

The development of the full grown tapeworm from the immature form released from the ingested cyst takes place wholly within the lumen of the gut.

There is no further invasion than this at any stage of its life history. A highly toxic product is developed which, when absorbed through the mucous membrane, has serious effects on the blood-forming organs and produces a primary type of anemia.

Diphyllobothrium mansoni.—The sparganum larvæ actively penetrate the stomach wall and migrate along the peritoneum to some underlying musculature or connective tissue where they multiply and form local swellings.

Dracunculus medinensis.—Developmental larvæ in the body of ingested Cyclops are activated by the gastric juice which causes them to work their way out of the body of this host into the stomach cavity. The freed larvæ penetrate the walls of the stomach or duodenum and migrate through the human tissues until they reach the subcutaneous tissues. Here they mature and the female when gravid then approaches and penetrates the deep layers of the skin and frees her larval progeny into the blister which develops at that site. The young are extruded into the external environment through a break in this lesion.

Echinococcus granulosus.—The newly-hatched embryo in the intestinal canal attaches itself by its hooklets to the mucosa and then penetrating it, invades a venule of the portal or systemic venous circulation. From there it is carried by the blood to the liver or lungs in which locations it is caught in the capillary network where it begins to grow and form a hydatid cyst.

Hydatid secretes a toxin which is largely retained within the walls of the cyst. It may escape by seepage through the walls and gain the systemic circulation or may be liberated by rupture of the cyst. Hydatid toxin produces a high degree of eosinophilia and elicits specific precipitins. It produces alexin-fixing bodies and is actively sensitizing.

Echinostoma ilocanum.—The developmental form of this fluke is presumably liberated from its cyst in the intestinal canal and attaches itself by its sucker to the mucosa where it grows to adult size. Nothing is known of its actual development or pathogenicity.

Enterobius vermicularis.—The rhabditiform larva is freed from the egg in the duodenum. It undergoes two ecdyses in the lumen of the intestine and when it reaches the colon attaches itself to the mucosa and grows to maturity. The mucosa at the points where the worms are attached shows an irritative inflammation which may go on to local necrosis. The nervous manifestations accompanying this worm are attributed to local irritation of the sympathetics and the action of a toxin.

Adult worms on the perianal skin may produce pruritis.

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Fasciola hepatica.—Adolescariæ emerge from the egg in the duodenal digestive juices and attach themselves to the mucosa. When they reach the opening of the common duct they invade it and actively work their way up to the smaller biliary capillaries. At this point they are stopped and there develop into adult flukes. They produce a cirrhotic reaction in the neighboring liver tissue and mechanically obstruct the biliary radicles. Absorbed toxin produces a severe anemia with eosinophilia.

Fasciolopsis buski.—The embryos, freed from the cyst in the duodenum, attach themselves to the intestinal mucosa where they grow to adulthood. Capillary hemorrhages may occur at the site of attachment and abscesses may be formed from inflammatory reaction to the flukes. Toxic effects are revealed by an eosinophilia, and in severe cases, by general anasarca.

Heterophyes heterophyes.—Nothing is known of the method of invasion or pathogenesis of this fluke after the adolescaria has become excysted.

Hymenolepis nana.—The eggs of the dwarf tapeworm hatch out in the small intestine and the young larvæ invade the villi. Here they develop into immature cercocyst forms which work their way out again into the intestinal canal. In a short while they fasten themselves to the mucosa and there develop into adults. The eggs from these adults can then develop in the intestine and complete the life cycle by auto-infection within the same host.

The pathogenesis of this worm is attributed to toxic effects on the nervous system producing reflex irritation and general nervous symptoms. Eosinophilia is a prominent finding.

Loa loa.—The microfilaria deposited on the skin by the mango fly rapidly enter the hair follicles and penetrate their walls thus finding their way into the subcutaneous connective tissue. The further development of the larvæ has not been traced but the adult worms are found most often in the subcutaneous connective tissues. Their presence is accompanied by localized, evanescent swellings, the pathogenesis of which is not known.

Onchocerca volvulus.—The microfilariæ deposited on the skin at the time of the bite of the buffalo gnat burrow into the skin and enter the subcutaneous tissues. The larvæ produce little if any evidence of pathogenesis but the adults produce proliferative subcutaneous nodules from which the worms can be recovered.

Opisthorchis felineus.

Opisthorchis viverrini.

Adolescariæ escape from the cysts in the duodenum and attach themselves to the duodenal mucosa. They migrate along the mucosa to the opening of the common duct and entering it move along the duct to the small biliary radicles. Here they develop into adults and produce an irritative desquamation of the biliary epithelium

with subsequent proliferative regeneration of bile capillaries and periportal sclerosis.

Paragonimus westermani.—The adolescaria excysts in the duodenal juice and actively penetrates the walls of the small intestine to the serosa along which it travels until it reaches the diaphragm. It then passes through the peritoneum, diaphragm and pleura and invades the lung tissue proper. When it reaches the bronchioles it ceases its wanderings and grows to adulthood. Aberrant migration may bring the larva to organs other than the lungs. They have been found in the liver, peritoneum, testicles, and brain, and located in muscles in various places about the body.

The adult fluke forms a thick-walled reactionary cyst about itself which may be relatively quiescent or may suppurate and ulcerate.

Toxic products may be absorbed. They produce eosinophilia and a positive alexin-fixation reaction.

Schistosoma hematobium.
Schistosoma japonicum.
Schistosoma mansoni.

The cercariæ of these three blood flukes on coming into contact with moist skin digest their way through it by means of histolytic ferments produced in their cephalic glands. From the subcutaneous tissue spaces they invade the blood-vessels or lymphatics and are carried directly or indirectly to the general circulation by passage through the lungs. The subsequent pathogenesis produced by the different types of parasites is common to all of them up to the time of maturation of the adult flukes and consists largely of local toxic reactions to the young larvæ in various tissues of the body where they become caught in the capillaries and general intoxication manifested particularly by fever and urticaria. Further pathogenesis is dependent on the ultimate tissues in which the adults mate and reproduce. *S. hematobium* reveals itself largely in lesions of the genito-urinary tract, *S. mansoni* in the walls of the intestine, and *S. japonicum* in the liver and biliary system.

Strongyloides stercoralis.—Filariform, infective stage larvæ actively penetrate the hair follicles and their lining cells and make their way into the subcutaneous tissue. In this location they either migrate along the lymphatics to the thoracic duct and reach the right heart or they invade capillary vessels and are carried to the right auricle by the blood stream. From the heart they are washed into the pulmonary capillaries from which they bore their way out and then through the pulmonary epithelium make an exit into the alveolar spaces. They migrate on or are moved along the bronchial surfaces to the trachea and larynx and on reaching the epiglottis and pharynx are carried down to the stomach with swallowed

materials. In the ileum they burrow into the superficial layers of the mucous membrane and grow to adulthood.

Larvæ may also invade the oral mucosa and initiate their wanderings from that point.

Invading larvæ produce an irritation dermatitis and a catarrhal enteritis. Adult worms have an irritating toxic effect on the submucous tissues and epithelial cells, particularly those of the intestinal glands.

Taenia saginata.—Viable cysticerci are liberated from *cysticercus bovis* by digestive action in the stomach and duodenum. The young worm attaches itself by its head end to the mucosa of the ileum and there grows to maturity. It produces a toxin which is responsible for the nervous manifestations.

Taenia solium.—Viable cysticerci are liberated from *Cysticercus cellularis* by digestive action in the stomach and duodenum. The young worm attaches itself by its head end to the mucosa of the ileum and there grows to maturity.

Viable eggs ingested and arriving in the duodenum and ileum and eggs produced *in situ* by an adult already present in the intestine may hatch out and the larvæ penetrate the intestinal wall. From here they invade the blood or lymph channels and are carried to many parts of the body, particularly the brain, orbit, muscles, liver, and lungs where they metamorphose to *cysticerci.*

A toxin is probably responsible for the nervous manifestations of the intestinal type of the parasite. Disturbances of glandular activity in the intestine may account for some of the gastro-intestinal symptoms.

Trichinella spiralis.—Viable larvæ liberated from cysts by digestion in the gastric juice or larvæ produced from a gravid female in the intestine actively invade the intestinal mucosa and enter small veins or lymphatics. They are carried to the heart, then to the lungs and back to the heart by passage through the pulmonary capillaries. From the left heart they are scattered throughout the body, but only those arriving in striped muscles find a medium favorable for survival. The diaphragm, tongue, and laryngeal muscles are most favorable.

The larvæ in the muscles undergo encystation where they may live for long periods of time even though the cyst walls may become calcified.

The adult worm in the intestine produces an irritative enteritis. The invading larvæ cause toxic myositis during the period of invasion of the muscles and severe systemic reactions with fever and a high eosinophilia. The reaction about the encysting larva is a degeneration of muscle fibers followed by a proliferative interstitial myositis.

Trichocephalus trichiuris.—Rhabditiform larvæ are liberated from the egg by digestion in the intestine. The active larvæ pass down the small intestine to the cæcum where they attach themselves to the mucosa and grow to adulthood. Some may invade the lumen of the appendix and develop there.

There is ordinarily no significant lesion at the point of attachment but occasionally the head end of the parasite may invade as far as the mucosa or even penetrate the serous coat. Such lesions open the way for invasion by pathogenic bacteria.

Other manifestations are probably due to local sympathetic irritation and reflexes, or possibly a general toxemia. A worm may cause mechanical obstruction of the lumen of the appendix.

Wuchereria bancrofti.—Mature larvæ deposited on the skin during the act of biting by an infected mosquito (*Aëdes*) rapidly invade the skin and reach the subcutaneous tissues. Here they invade the blood-vessels and are carried by the blood stream throughout the body. Where they lodge, they leave the blood-vessels and enter the lymph spaces and channels. In these places they mature to adult males and females and reproduce offspring as microfilariæ.

Pathogenesis, if produced at all, is due to mechanical blockage of lymph channels or vessels (chylous ascites, elephantiasis of different organs and parts, chylocele and lymphatic varices) due either to the accumulation of the worms themselves or the worms plus a fibrous, proliferative reaction in the lymph tracts and lymph glands. The adult filariæ may damage the intima of small blood-vessels and permit invasion of the arteries and veins by circulating bacteria. This secondary infection is probably responsible for much of the inflammatory reactions in elephantoid lesions.

Arthropods.—The larvæ and adults of these parasites possess, for the most part, well developed predatory apparatuses by which they can cling to human tissues or burrow their way through them. In addition, many of them possess secretions from some parts of their bodies which are irritant and toxic. Those species which produce disease in man only by virtue of these toxic principles act in reality as sources of exogenous poisons and are therefore more accurately placed under that category. Others, however, produce pathologic changes by virtue of other life activities and are considered in the present section.

The mosquito penetrates the normal skin with its proboscis and in so doing produces minute openings for the entrance of bacteria. Secondary infection is far more likely to occur through excoriations made by scratching. The so-called immunity to mosquitoes shown by some people is probably a question of differences in sensitization and not true immunity.

Ticks attach themselves to the skin by their mouth parts in the act of obtaining a blood meal. Their bite may cause minute hemorrhages, and secondary infection can occur through the wound and the small papule and vesicle which develops from the irritation. Young adult female ticks may, under poorly understood circumstances, be the cause of a severe and frequently fatal acute ascending motor paralysis. It is not known whether this is due to a secretion elaborated by the salivary or reproductive glands of the tick. Species of *Dermacentor* and *Ixodes* have been found to be responsible for tick paralysis.

The members of the genus *Trombicula*, or the itch mites, and *Pediculoides ventricosis*, the grain itch-mite, attach themselves as larvæ to the superficial layers of the skin. Only the mouth parts penetrate the skin. The local inflammatory urticarial reaction at the site of the bite is believed to be due to the irritant action of their saline saliva. Secondary infection may occur through the wound, especially if it has been traumatized by scratching.

Phthirius inguinalis, or the crab-louse living on the pubic or other hair feeds from the skin and in so doing irritates it by some unidentified secretion. It has been suggested that the pigment either of the louse body or its feces is the irritating factor.

Pediculus attaches itself to the skin only during feeding. It produces a mild, evanescent urticarial response.

The adult female larva of *Sarcoptes scabiei* is able to burrow its way into the superficial layers of the skin. Some irritating secretion is responsible for the intense itching and probably also for the low-grade inflammatory reaction along the course of the burrow. The female lays eggs in the burrow in which the young hatch as larvæ and extend the burrow on their own account.

Cimex produces local urticarial wheals due to some secretion placed in the wound made by the mouth parts in the act of biting.

Glossina and *Pulex* produce an ordinary irritating, stinging bite without any special pathology attached to it.

The majority of the cutaneous myiasis-producing flies develop from eggs deposited in the secretions, discharges and dead materials on the surface of the body or in the superficial cavities. They are made up mostly of the bot-flies and warble-flies and occasionally the domestic house flies. The young larvæ or maggots penetrate the soft material in which they are hatched and on reaching the neighboring tissues are able to invade it for greater or lesser distances by means of their lateral hooks protruded through the mouth parts. Most of them are aided in all likelihood by proteolytic ferments which they elaborate, and the softening action of accompanying bacteria. *Chrysomia macellaria*, the common screw-worm, is able to invade normal tissues and even bone. The Old World screw-worm, *Chrysomia bezzianum* can only penetrate devitalized

tissues. As fly larvæ bore their way through tissues they cause active destruction of the cells with necrosis and ulceration. Secondary bacterial infection is generally present and produces pus. Large accumulations of larvæ may obstruct nasal and aural passages. Screw-worms have been found burrowing deep into body tissues and have been recovered from the interior of bones and the brain. Some sensitization is produced.

The larvæ of the bot-flies *Cordylobia anthropophagia* and *Dermatobia hominis* and of the warble-flies, *Hypoderma bovis*, *Wohlfahrtia magnifica* and *Wohlfahrtia vigil* can penetrate unbroken normal skin. They burrow through the superficial connective tissue layers but do not go deeper because they must remain in ready access to air.

The larvæ which produce intestinal myiasis in man are not adapted to any prolonged parasitic existence and are in the intestinal canal only through accidental ingestion as larvæ or matured eggs. They may attach themselves temporarily to the intestinal mucosa and produce minute hemorrhages. The bot-fly larvæ are the ones most readily able to survive passage through the human alimentary tract. Massive accumulation of larvæ may cause some degree of intestinal obstruction.

Aural, nasal, orbital and urinary myiasis are caused by the same representatives of fly larvæ as produce cutaneous myiasis, their special location giving them particular significance.

CHAPTER XLIII.

THE INTERACTIONS BETWEEN HOST AND PARASITE.

THE reactions of the human organism to the vital activities of lesser organisms which are able to invade it are far from being entirely advantageous to the host. A casual consideration of the elements of pathogenesis outlined in the previous section will show that the invaders have produced damage of varying degrees—the essence of the meaning in pathogenic parasitism. There are however certain aspects of the host reactions which have a distinct bearing on the success of the invasion and influence the host in its behavior toward the entrance of similar or closely allied organisms at some subsequent time. The present discussion is not concerned with those organisms in the environment of man which are positively unable to invade him. There are many such parasites of lower animals to which man is genetically insusceptible, not necessarily through the processes of immunity in the restricted sense of the term, but because the genetic associations of the past have never worked toward such possible interactions. Nor is there any interest at the moment in the organisms which parasitize man and produce no disease, reserving the privilege however of anticipating the *possibility that the future of man and the non-pathogens may* involve changes which will operate to bring about some harmful relationships.

All host-parasite reactions are primarily cellular, that is they are initiated by cellular activity and this in turn is chemical in nature. No exceptions are evident at this time to this broad generalization. Where it is contended that physical and mechanical forces are involved, analysis reveals that these forces may act to produce changes in kind but when the materials acted upon *react* it involves chemical activities in the cells directly or in their products. The puncture of the skin or mucous membranes by metazoan parasites, for example, is more than physical; it involves reactionary chemical changes in the cells whose equilibrium has been disturbed, and this occurs even without the inclusion of additional toxic substances in the process.

Nowhere in the medical sciences is there so great a tendency to confuse the explanation of a process with its description as in the subject under consideration. On every hand in immunology, serology, and cellular pathology, end-processes have been set up as

entities and endowed with the virtues of causality. Precipitins, agglutinins, opsonins and so forth have been made to appear as deliberate purposeful agents which are able to perform such functions as their names connote, whereas there is at present no evidence that any one of them is strictly speaking either purposely defensive or even an isolable independent entity. Recent chemical investigations have shorn them of much of their former attributes and brought them down to the level of complex manifestations of understandable chemical processes.

THE PART PLAYED BY THE PARASITE.

As the development of the discussion on the host-reactions to disease agents proceeds, it will be noted that the tendency is to bring many of the observed processes back to the causative agent for explanation. Thus, although the term *antigen* has been in use for many years and its etymologic meaning has been well understood the "anti" fraction has been overemphasized at the expense of the whole word. That an antigen is an agent which calls forth reactions to it does not necessarily make it possible to examine the elements of the reacting substances as though they existed independently of the agent which produced them and on which they react. This ancient conception is fortunately being overthrown.

All antigens are believed to be protein, contain protein, or be intimately associated with proteins. This is true, however, only of the whole antigen.

Fractional analyses of antigenic substances have shown them to be complex molecules or molecular aggregates, some part of which probably must be protein but the remainder may be of one or more different types of simple or complex chemical substances. The non-protein fraction called the hapten cannot by itself stimulate anti-antigenic substances (Antibodies). The protein fraction or *protein component* is the actual stimulator of antibody production.

A brief review follows of the origin and nature of the antigenic and reacting substances so far identified with the host-parasite relationship, and the mechanisms of the processes involved.

Antigens are of two kinds—complete and incomplete. A *complete antigen* according to the most modern concepts is defined by Gay as any agent which when introduced into the body combines the power of inducing antibody production with the capacity of reacting with the corresponding immune bodies. *Incomplete antigens* or *haptens* cannot stimulate the production of immune bodies but have the ability to react specifically to them *in vitro*.

Haptens may be either *simple haptens* or *complex haptens*. The simple hapten is one which unites with antibody forming a com-

pound that remains in solution; a *complex hapten* unites with an antibody to form a precipitate in the test-tube.

As it is still impossible to define an antibody with complete accuracy it is evident that the above definitions, expressed in terms of antibody production, may have to be changed later as the nature of antibodies becomes clearer.

Complete antigens, as expressed previously, are protein complexes with large molecules of very high molecular weight. This is stated with the reservation that certain non-protein substances given parenterally result in antibody production but it is not yet proven that these simpler materials do not combine first with some body protein before initiating the reaction.

As implied in the definitions the complete antigen or its "protein component" is the antibody stimulant whereas the hapten, by virtue of its combining powers with the antibodies so produced and those special antibodies alone, provides the specificity of the antigen-antibody reaction.

It has been demonstrated that the hapten may be one of many kinds of chemical substances—polysaccharid sugars,[1] azo-compounds,[2] arsphenamine,[2] anilines,[3] nitrobenzenes,[2] iodine[2] and lipoids.[3]

Antibodies have been demonstrated to result from the introduction into the human body of many forms of living disease agents. This is particularly true of the bacterial microörganisms and viruses but has also been shown in the case of some of the higher forms of life. Interest is now centered largely on the point of origin of the antigens responsible for these antibodies—that is, from what part or parts of the body of the parasite are they liberated and how do they become free to act?

Chemical investigations of the bacteria have revealed the presence of antigenic substances in their flagellæ and different parts of their bodies.

Although Beyer and Reagh[4] had identified the existence of distinct antigens in the flagella and cell body of the hog cholera bacillus as early as 1904 it was on the work of Weil and Felix[5] in 1917 that the flaggellar antigens became designated by the letter H and the somatic antigens by O (H standing for *hauch* and O for *ohne hauch*—with, and without "exhalation" growth, respectively, on culture media).

It has also been found that the S and R (smooth and rough) variants of bacteria described by Arkwright[6] differ in their antigenic

[1] Heidelberger, M., and Avery, O. T. Jour. Exp Med., 38, 73, 1923.
[2] Landsteiner, K.: New England Jour. Med, 215, 1199, 1936.
[3] Forssmann, H.: Handb. d path Mikroörg, 3d ed, Berlin, vol. 3.
[4] Beyer, H. G, and Reagh, A. L. Jour. Med Res, 12, 313, 1904
[5] Weil, E., and Felix, A.. Wien klin. Wchnschr, 30, 1509, 1917.
[6] Arkwright, J.: Jour Path. and Bacteriol, 23, 358, 1920, Ibid, 24 36, 1921; Brit Jour. Exper. Path, 5, 23, 1924.

structure and that this in turn is correlated with the presence or absence of certain antigenic grouping at different points on or in the bacterial cell.

A variety of graphic representations have been utilized to show the assumed location of the different antigens in the bacterium but Topley[1] gives a timely warning that "a diagram is not a picture and that by placing an antigen at the cell surface we are implying that it behaves as though it were there and by placing it beneath the surface we mean that it seems, in the normal form of the organism, to be overshadowed by some other bacterial component."

Nevertheless there is now no doubt that the accessibility of some antigen components to the action of specific antibodies is greater than others and that this has an important bearing on the types of reaction that can occur. Variations in this make-up occur under natural conditions in the dissociation of bacterial types and are accompanied by measurable differences in virulence. In general the S types are more virulent than the R although there are exceptions.

The reader must be referred to the original articles for a full description of these phenomena or to the excellent summaries in the more recent bacteriology texts.

A single example in the pneumococcus will be given to show the application of these principles to a specific organism. (Taken from Topley.[2])

The haptens of the pneumococcus as isolated by Heidelberger and Avery are probably confined to the capsule. They are: in Type I pneumococci—Galacturonic acid and amino-sugar derivative; Type II—Glucose; Type III—Glucose and glucuronic acid. The loss of the capsule means the loss of these haptens and the type specific reactions of the organisms. The same investigators found also a nucleo-protein fraction which gave a precipitate with antisera corresponding to each of the three types. This antigen is believed to lie beneath the capsule.

The change from Smooth to Rough colonies is a change from the encapsulated state to the non-capsulated and from virulence to avirulence.

When the antigenic faculties of an organism are looked at from the standpoint of the types of observable reactions which they elicit they are called by such terms as agglutinogenic and antitoxigenic, or bacteriolysin-, hemolysin-, and precipitin-producing.

Animal and vegetable parasites in many classes of their respective kingdoms possess in their substance, or elaborate, certain protein constituents which when introduced into man reveal themselves

[1] Topley, W. W C.: An Outline of Immunity, London, Edward Arnold & Co., 1933

[2] Topley, W. W. C An outline of Immunity, Baltimore, William Wood & Co., 1933.

by reactions on the part of the host which are designated as toxic. These toxicity-producing substances are called *toxins*. Those under consideration in this section are all derived from organisms which actually parasitize man, distinguishing them therefore from those which cause intoxication without parasitism (cœlenterates, ants, bees, wasps, snakes, etc.) and are dealt with in the section on Exogenous Chemical Agents.

Beyond the fact that these parasitic toxins are probably all protein in nature little is known of them other than what is revealed through their behavior. They are, with important exceptions, antigens and therefore come within this class of parasite products.

In the bacteria they are divided into exotoxins and endotoxins. The former are elaborated and freed into the bacterial environment during the life of the parasite and thus behave *as though* they are secreted by the bacterial body. This connotation is not only unnecessary, but probably erroneous and until more is known of their nature and mechanism of production, should not be read into their behavior. The exotoxins are pharmacologically active and antigenic. They are specific and possess characteristic affinities for particular host tissues. These differences are the only ones known which account for the differences in the symptoms produced by the invasion of specific bacteria. Their outstanding antigenic characteristic is their power to stimulate the production by the host of specific antitoxins which can neutralize them.

Endotoxins are vaguely defined toxic substances closely if not permanently associated with the bacterial cell during its life. Because they are revealed only on the disintegration of the cell it has been assumed that they are in the cell and not liberated into the environment during cell life. This assumption is being challenged but the term endotoxin is retained as a working hypothesis because it sets up a distinction between those poisons which are diffusible in the media and can be obtained apart from the live cell by filtration and those that cannot.

Endotoxins are weakly anti-toxinogenic or not at all. They are, however, antigenic in other ways such as in the stimulation of hemolysin formation. Their toxicity is of a much lower degree than that of the exotoxins.

The majority of the viruses are antigenic and call forth the formation of anti-viruses which are collectively referred to as neutralizing antibodies. It seems probable that only living active viruses are able to stimulate antibody production. There is evidence from the fact that there are three types of foot-and-mouth disease virus, that viruses might possess different antigenic patterns. That they are protein is unquestioned but it is yet to be proven that non-protein haptens are present and account for specificity. Nevertheless, the tendency is to accept the little

evidence at hand that viruses may possess antigenic structures analogous to if not similar to the bacteria. No soluble toxins have been found in connection with any of the viruses, the organisms' presence in close association with living cells being the only mechanism of pathogenesis recognized so far.

Inadequate information about the nature and structure of the *Rickettsiæ* makes it impossible to give any real indication of their antigenic powers. The effective immunity which results after infection with *Dermacentroxenus rickettsiæ* and *Rickettsia prowazeki*, the cross agglutination of the typhus organism with *Bacillus proteus* X19, and the fleeting immunity which appears to be present between relapses in Tsutsugamushi disease and trench fever are strongly presumptive of definite antigenic properties.

With the exception of *Treponema pallidum* and *Treponema vincenti*, all of the spirochetes are proven producers of humoral antibodies of the nature largely of agglutinins and lysins. They are highly type specific. No exotoxins have been demonstrated although the clinical evidences of infection by these organisms indicate considerable toxicity.

The antigenic properties of the fungi are almost entirely limited to the production of substances which cause specific agglutination responses or tissue sensitization. Both of these are highly variable among the members of the class but are held generally by representatives of some of the genera.

Fungi Which Elicit Agglutination Responses.

Epidermophytons.	*Coccidioides immitis.*
Endodermophytons.	Sporotrichum.
Monilia albicans.	Actinomyces.

Some few of the fungi produce a toxic substance which is not primarily active at the time of first invasion by the parasite. They only manifest their toxicity in individuals who have developed sensitivity through previous exposure to them. This departure from the behavior of true toxins has resulted in giving them the name *Toxallergens.*

Fungi Which Elicit Sensitization.

Epidermophyton.	*Monilia albicans.*
Endodermophyton.	*Coccidioides immitis.*
Trichophyton.	Sporotrichum
Torula histolytica.	

Of the pathogenic *Protozoa* only *Leishmania tropica* and *Trypanosoma gambiense* give any evidence that they can produce anti-

body immunity and this rests on clinical grounds alone. What poisonous products they give off or cause in the tissues of the host appear to act directly without intermediation of antitoxic or other substances; they are therefore not true toxins or toxallergens.

Ascaris lumbricoides, *Echinococcus granulosus* and the *Schistosomata* are parasitic *Helminths* which possess sensitizing powers, probably through elaboration of allergy-producing toxins. In these and all other helminths there is no evidence of any antibody immunity.

The higher metazoan parasites among the *Arthropods* are neither generally sensitizing nor immunizing. Although mosquitoes, bedbugs, ticks and some cutaneous myiasis-producing flies show local urticaria-like lesions at the site of the location of the parasite these responses are similar to the effects of the zoötoxins of non-parasitic agents of the same class of animals.

The non-antigenic poisons produced from the protoplasm of living or dead parasitic agents cause local, general and special tissue reactions which form an integral part of the whole picture of the disease in which they are implicated. These fractions of the total pathogenic agents are best looked upon however, as intoxicants. They are as a rule simpler compounds than the antigens and may even be simple chemical substances. Probably all pathogenic parasites possess some such substances which are more or less toxic to their hosts. They may be an important factor in their primary invasion and subsequent local tissue effects. When some of the larger compounds are looked at and an analysis is made of the reactions which they bring about they are seen to approach and actually overlap in some respects the phenomena of antigenesis. It is well therefore that not too strict a dividing line be made at this point and to wait for clarification by further advances in the science of immunology especially in respect to sensitization phenomena.

A series of observations commencing with those of Bail in 1900 and continued by others up to the present have shown that when virulent bacteria gain admission to normal human tissues containing polymorphonuclear leukocytes, the leukocytes move away from the vicinity of the organisms as though they were being repelled. Bail believed that this negative chemotactic effect was due to the action of a bacterial product which he called *aggressin*. More recent terms applied to the same hypothetical substance are *virulin* (Rosenow) and *antiphagine* (Tchistovitch and Yourevitch) all of them unfortunate normative expressions which Topley would correct by speaking only of the effect and calling it the *aggressive action*. Although filtrates can be obtained free of organisms which manifest this activity no substance has been identified with it. Gay and Topley express the view that they may be soluble haptens, com-

plete antigens, or endotoxins. They are not specific but are believed by the same authorities to have some influence in bringing about an anti-aggression effect. Weak and non-virulent organisms do not show aggressive action but on the contrary exhibit positive chemotaxis toward leukocytes.

Materials of somewhat similar nature in respect to their probable origin but which are destructive to leukocytes are also found in bacterial exudates. These so-called *leukocidins* are toxic to the leukocytes after the organisms have been phagocytized by them. They are especially active in the virulent staphylococci and streptococci. They are apparently soluble toxins which are capable also of eliciting anti-leukocidins.

Enzyme activity has long been known to be a common property of bacteria, and enzymes are frequently mentioned in the description of the vital processes of fungi, protozoa and some metazoan parasites. The question has been raised but not answered as to what part these enzymes play in pathogenesis and resistance to infection. The following, from Topley (Outline of Immunity) succinctly expresses the possibilities: "It is reasonable to suppose that the occurrence in the tissues and body fluids of catalyzed chemical changes, proceeding independently of the normal body *metabolism, might seriously interfere with the host's nutritional* economy. It seems quite possible that, whenever there is formed in the tissues a nidus of bacterial cells, alive or dead, there may result in the immediate neighborhood a diversion of the normal metabolic processes sufficiently serious to derange the local cell-activities. It is not impossible that the diffusion of bacterial enzymes might convert such a local effect into a more general one.

"Should such factors be found to be concerned in the reaction between parasite and host they would consort well with our knowledge of certain aspects of infection and resistance. Thus it seems to be fairly definitely established that ferments are relatively ineffective antigens, that is, they fail to stimulate the formation of neutralizing antibodies when injected into the animal tissues, or do so only to a minimal degree. In this they share the characters of many so-called endotoxins."

THE PART PLAYED BY THE HOST.

The host which is subjected to the action of the antigens of its parasite produces somewhere in its tissues a substance (or substances) which reacts to this foreign material and is called an *antibody*. It appears best to think of the antibody as a reacting agent which appears only as a response to the activities of the antigen and to soften the emphasis on the implication that it is an antagonist.

It has almost definitely been proven that antibody is protein and probably a globulin or variation of it. The chemical analyses of serum antibodies undertaken by all investigators of the problem have invariably revealed that antibody is protein and so far as can be determined is not separable from the serum globulin. Carried to its farthest practicable fractionation it remains indistinguishable from globulin except in that antibody globulin is slightly more basic than normal globulin. It was suggested by Buchner that antibody specificity was accounted for by the inclusion of some of the antigenic substance in the antibody complex. This assumption appears to have been proven wrong by the work of Heidelberger and Kendall[1] who showed that the antibody to a red azo protein (R-salt-azo-benzidine-azo crystalline egg albumin) antigen was not red, as was the specific hapten, but colorless. Beside this colorimetric test the same authors determined that the quantity of antibody produced from a minimal amount of antigen could not be explained by the participation of specific antigen fragments in the antibody. This has further corroboration in the work of Marrack,[2] who showed that diphtheria antitoxin behaves as though it were identical with serum pseudoglobulin and the amount of floccules precipitated by diphtheria toxin-antitoxin reaction is independent of other serum proteins present or added.

If it can be assumed that antibody is a function of globulin the problem arises as to what may be the nature of the change in the normal serum globulin by which it is endowed with this acquired attribute.

Breinl and Haurowitz[3] conceive that the antigen acts at the point of formation of serum globulin in ways indicated by the specific nature of the antigen so that when antigen and antibody meet they are enabled to interact in a specific way. Mudd[4] expresses a similar idea. For him it is a stoichiometric or absorptive process between the antigen and the elemental units out of which the globulin is built so that the new antibody-globulin has a stereochemical correspondence with the antigen and is therefore specific for it.

These hypotheses can hardly be expected to hold unaltered under the acquisition of new knowledge but they do in their general implications point to very likely possibilities. The information on which they are built and many other data undoubtedly are directing the trend away from the time-honored side-chain theory of Ehrlich, at least in this respect.

[1] Heidelberger, M Contributions to Chemistry to the Knowledge of Immune Processes, Harvey Society Lect., New York City, March 17, 1933. Medicine, 12, 279, 1933.

[2] Marrack, J R · Chemistry of Antigens and Antibodies Med. Res. Counc, His Majesty's Stationery Office, London, 1934.

[3] Breinl, F., and Haurowitz, F.: Ztschr f physiol Chem, 192, 45, 1930.

[4] Mudd, S.: Jour. Immunol., 23, 423, 1932.

On the evidence at hand and visualization of the possible processes as outlined above it is impossible to do more than guess at the point of origin of the antibodies. It is not known for instance where serum-globulin is synthesized. There is strong evidence that antibody formation may be a function of the elements of the reticulo-endothelial system. Cells of other tissues have not been denied the possibility of participating in antibody formation but the case for them does not rest on as impressive grounds as does that for the reticulo-endothelium. It would be much beyond the scope of this work to record the details of the controversy on this point. Discussion of the manifestations of antibody activity will be delayed until after consideration of the remaining responsive parts played by the host.

One of the oldest responsive activities of the host, historically, is the behavior of the leukocytes in the face of foreign antigens. Factually it is observed that the leukocytes increase or decrease in numbers, either locally or generally, in the presence of an antigen. There is furthermore a qualitative change in the types of leukocytes present in the vicinity of the invading substance and this or other changes may also occur in the systemic circulation. There is a tendency for certain groups of antigens to stimulate similar but not necessarily specific pictures of leukocytic response.

It is now quite certain that the local manifestations are due to chemical attraction or repulsion between the antigen and the leukocytes. (Repulsion has been dealt with in the consideration of aggressins, page 478.) Attraction between the antigen and leukocyte is ascribed by Wells to lowering of the surface tension on the side of the leukocytes directed toward the antigen. This positive chemotaxis, aided by the active ameboid movement of the leukocyte, causes the white blood cell to approach the invader. It is therefore a vital, active response on the part of definite, free, cellular elements of the host.

The leukocytes most actively engaged in the process of *phagocytosis* are the polymorphonuclears and wandering macrophages. Their freedom of motion and the extrusion of pseudopods represents a fluidity which permits them to respond in such a way that, continuing to follow the laws of chemotaxis, they not only approach the bacterium or other foreign antigen, but flow over and around it until the invader is engulfed in the protoplasm of the leukocyte. In this position the antigen-bearing body is open to the influence of leukocytic enzymes, and if susceptible to them is destroyed.

Fixed tissue cells and especially the sessile macrophages of the reticulo-endothelial system also phagocytize. Their enzymes are believed to differ in type from those of the polymorphonuclear leukocytes.

Although, among the bacteria at least, many of the organisms are

destroyed by phagocytosis this is not an inevitable result and phagocytosis is not tantamount to destruction of the antigen. In some instances to be discussed later such intra-cellular existence may protect the organisms from harmful extracellular environmental factors.

Among the higher organisms such as the protozoa, the clasmatocytes are more particularly stimulated by the antigens and in the helminths the response is represented by an increase in the circulating eosinophiles. Sensitizing phenomena in allergy are frequently characterized by eosinophilia.

Normal human serum contains a substance called *alexin* or *complement* which is an important essential element in the functions opposed to the action of foreign antigens in the host. It is chemically a complex protein made up of albumin and globulin and probably two more fractions as yet unidentified. Although the known activities of alexin will be considered in more detail later it can be stated here that the whole alexin is alone able to operate against introduced antigens. That is, neither the albumin nor the globulin by themselves can consummate the actions attributed to the whole alexin.

From all evidence at hand alexin is not produced by the action of any known antigen but appears to be a part of normal serum and originates in the body as the result of normal physiologic processes. It is thermolabile and is made inactive by heating at 55° C. for one-half hour. It may also be inactivated by mechanical agitation. The claim that it is an enzyme is based almost entirely on its thermolability so that its identification with the enzymes is not firmly established. The source of alexin has not been determined. There are proponents of Ehrlich's view that it is a normal product of leukocytes but this contention as attractive as it is has not been supported by scientific evidence. For full discussions of this interesting body the reader is referred to the contrasting views presented by Ehrlich and Bordet and the work of Pfeiffer, Gay and others.

Most of the antigen-antibody reactions are dependent on the presence of alexin. These are discussed in the next section.

Parasite ⟷ Host Reactions.—In the preceding sections consideration has been given to the fundamental substances which are a part of or produced by invading organisms, and those present in, or caused to be formed by, the host.

Under natural conditions the antigens are introduced into a host with living organisms and their presence results in the formation of antibodies which react in turn upon the antigens. Antigens can be separated by various procedures outside of the host from the organisms which formed them, and the antigens so obtained may then be introduced artifically into the tissues of an individual who may or may not have had previous experience with these particular

antigens. Or host material and antigens may be caused to react together in the test-tube, the antigens remaining intact in the organisms or separated from them.

These three possibilities outline the important methods of observing the reactions between host and parasite materials.

In the living host with living pathogenic organisms which have gained admission to it the observable phenomena produced by antigen-antibody reactions are manifested by lysis and phagocytosis of the invaders and neutralization of their toxins. These phenomena are explained most satisfactorily by a process which has been simplified to a few generalizations which appear at present to have *withstood the test of scientific proof.*

Commencing with the *antigen*, it has been previously stated that the *protein component* stimulates the formation of *antibody* by the host and that this appears to be of the nature of a globulin, which is synthesized in a particular way under the influence of the *specific haptens* present in the antigen. A reaction now takes place between the specifically formed antibody and the specifically determined hapten of the whole antigen which results in chemical changes that *sensitize* the organisms on which the reactions occur to the action of *alexin* which was normally present in the host even before the arrival of the antigen. The result to the organism is determined by the location of the antigen-hapten compound in or on the body or other parts of the organism.

Lysis of the organism occurs when the antigen-antibody combination takes place on the surface of the body of the organism (bacterium) where the antigen is a fixed part of the cell structure. It occurs only in the presence of complement to which the organism is susceptible.

Phagocytosis of the organism is enhanced by opsonins developed by the host in response to the antigen. These antigens sensitize the bacterial or other cell to the action of the wandering and fixed phagocytic cells of the host. Opsonins are formed when the antigen-antibody combination takes place on the surface of the invading cell body.

Neutralization of toxin by a specific antitoxin takes place in the circulating fluids of the body. The toxin being itself antigenic stimulates the formation of its specific antitoxin. Toxin (exotoxin) and antitoxin, both of which are present in the fluids and separate from the cells which produced them, undergo direct combination which results in the neutralization of the toxin. This reaction is therefore entirely independent of the location of the toxin in the bacterial cell other than the requirement that it be an exotoxin. (It has been observed earlier in this work that endotoxins as here considered are non-antigenic.)

These happenings are all in favor of the infected host for they

mitigate against the growth and multiplication of the invaders and are antagonistic to the action of their poisons. For this reason the antibodies concerned are called *protective antibodies* and form an important part of the defensive mechanisms of the host. Phagocytized cells are further acted upon by the processes of the leukocytes and eventually cleared from the body of the host as are all other inert foreign materials.

The rate of formation of antibodies following introduction of antigens varies with the quality and amount of the antigens. It is not immediate but is characterized by a lag period and then the appearance of the antibody in increasing titres within the next two or three weeks when it attains its maximum. From then on it declines at varying rates. It may disappear entirely within a few months or persist for years. When a host is again subjected to the same antigen responsible for the formation of the specific antibody on the previous occasion, the body responds more rapidly in the production of new bodies than before. This "training" is sometimes referred to as the *anamnestic reaction* as though the tissues remembered what was expected of them! The result of this persistence and re-formation of antibodies is one phase of *Immunity.*

The sum total of bacteriolysis, phagocytosis, destruction of phagocytized bacteria and their removal by the reticulo-endothelial elements constitutes the clearing mechanism of the body. Although these results are more clearly seen against invading bacteria the same mechanisms are involved in the protection against other organisms wherever it is found that their antigens stimulate the formation of lysins, opsinins and antitoxins. It is present in the case of the viruses and has been demonstrated against some of the treponemas, is strongly suspected in the case of the rickettsias, is presumptive among a few of the protozoa (leishmania and trypanosoma), but has not been identified in the fungi, helminths, or arthropods unless consideration is given to the reactions following the introduction of their toxallergens.

From the foregoing discussion it is seen that the main mechanisms of defense, at least after invasion has occurred, are functions of both the cells and fluids of the host—a unity of action which has correlated the facts in the old controversy between cellular and humoral immunity. This is not to be confused with the question of local (tissue) *versus* general immunity. Local immunity is the resistance of a given area or a given tissue and may itself be evidence of cell activity and antibodies brought into the area from the general circulation or produced *in situ*. Strict interpretation of tissue immunity would require that any (or all) cells are capable of combining with antigen (fixation). This belief is being strongly pressed by Kahn[1] but his contentions have not been fully established.

[1] Kahn, R. L., Tissue Reactions in Immunity, XIV, Science, 79, 172, 1934.

Nevertheless, the reported results of this investigator's studies demand serious consideration.

When a human host becomes invaded a second time by a given organism he frequently exhibits certain reactions not present at his first experience with the antigen. The general nature of this reaction gives an appearance as though the host were particularly sensitive to the organism and the phenomenon as a whole has been termed *hypersensitiveness.* It is a highly variable reaction even under what appear on the surface to be similar circumstances. The variations are now believed to depend on the nature and dose of the antigen, the tissues through which it is introduced, the time elapsed since the previous experience with the same antigen and probably other factors such as diet, constitutional inherited factors, and others not yet determined.

Since only living agents of disease are now under consideration it is necessary only to remind the reader that hypersensitiveness to antigens other than those of living agents is a frequent occurrence and is embraced under the reactions known as anaphylaxis, anaphylactic shock, allergy, drug idiosyncrasies and atopy.

A discussion of the clinical manifestations of these conditions would be out of place in this book but it is necessary to outline the current views on the underlying mechanisms and processes involved.

In the first place the tendency is to unify all of the phenomena under the single heading hypersensitiveness. This is done on the assumption that the basic mechanism which involves antigen-antibody reactions is common to all. It is admitted at the same time that complete proof of this unity is lacking. However, the similarities in those aspects which have been investigated most thoroughly appear to outweigh the differences and point strongly in favor of a single mechanism with variable manifestations. A further step has been taken to link hypersensitiveness with immunity. This too has important points in its favor which, if upheld would lead to a true Unitarian Hypothesis.

Hypersensitivity to living organisms is specific; that is, the second experience must involve the same specific antigen that produced the sensitivity in the first place. In the case of bacteria it is fairly well established that the antigen produces an antibody response and that the antigen-antibody reaction takes place on or in the cells of the host. This results in the removal of the antibody from circulation which is consummated in from eight to twelve days. At a time subsequent to this interval the introduction of an antigen similar to that of the first reaction will now produce a new type of reaction which apparently is due to a sensitive state induced in the host cells by the former antigen-antibody reaction. The result seems to be harmful to the cells and the injury brought about is characterized by the formation of some toxic split-protein product

derived either from the cell, the antigen or both. The histopathologic picture at the site of the reaction is highly suggestive that the toxic agent responsible for it is histamin or a histamin-like substance. This same substance produced in larger amounts may be carried by the circulation and brought in contact with histamin-sensitive cells. The injury induced in them could readily account for the phenomena of anaphylactic shock.

The local reaction is inflammatory and exudative in character. The exudative reaction in tuberculin sensitive tissues brought about by the introduction of new tubercle bacillus antigen or its sudden increase or spread in the body is the classical example of this kind of reaction.

An excess of antibody in the circulation protects the antigen-antibody combination on the cells and inhibits any allergic reactions while the excess persists. While this protection lasts, no acute reactions to new antigens can occur. This refractory period is termed *Desensitization*. It is not permanent but wears off as rapidly as the antibody becomes removed from the circulation. When entirely removed the tissues become as susceptible as before and persist so probably for the rest of the individual's life. Desensitization can be artifically induced by the introduction of more antigen during the period when the first antigen-antibody fixation is taking place because this results in excess circulating antibody which does not permit the new antigen to affect the cells.

Friedberger's original "anaphylotoxins" were believed to be formed in the circulation as a result of the combination of antibody with antigen in the presence of alexin. This new split-protein product was then held to be responsible for the symptoms of anaphylaxis. The theory of the cellular origin of the toxic material is proving to be more popular than this historically older conception. Nevertheless the circulatory source of the reactors in some of the hypersensitive states is not denied. It may be that the mechanisms of anaphylactoid reactions and drug idiosyncrasies depend on changes taking place primarily in the blood serum.

Hypersensitiveness is generally looked upon as detrimental to the host and it cannot be doubted that this may be so in some of its aspects. It must certainly be so in anaphylactic shock which follows a sudden increase in antigen in the body, usually the result of its introduction by artificial means. But looked at in its entirety and especially in its relation to the local inflammatory peculiarities accompanying it, it is difficult to divorce this antigen-antibody response from the immune processes which seem to depend on a similar mechanism. Local tissue immunity already has considerable proof of its existence and cellular immunity is being seriously considered. Hypersensitiveness may readily partake in both of

these complexes and in ways not yet known enhance the ultimate outcome in favor of the host.

For more detailed discussion of this subject the reader must refer to the more exhaustive contributions of Coca,[1] Dale,[2] Gay,[3] Landsteiner,[4] Weil,[5] Doerr,[6] Sulzberger,[7] and others.

Immune bodies which are effective against human pathogenic organisms can sometimes be produced in the bodies of other animals. This is accomplished by artifically subjecting such animals as the horse, goat and smaller laboratory animals to living organisms or their products. By varying the dose of the antigenic substance and controlling the frequency of administration, or by selecting more or less virulent strains of the organism, the animal may be forced to respond to a degree greater than that resulting from natural infection. The serum or other tissues of the animal in which the responsive bodies may be found can then be taken from the animal and after treatment of many kinds administered to man. Since these animal antibodies have been formed in response to human pathogens they will be specific for them and add to the quantity of similar specific antibodies in the tissues of man, or, if he has never before produced such specific protective substances, the animal antibodies will act for them.

Many pathogenic bacteria can be grown on artificial media outside of the body and their antigenic products used to stimulate antibody formation in man. The antigen as used may remain in the bodies of living organisms, but when this method is used the bacteria must be of a naturally harmless strain or rendered less virulent by different culture procedures, or may be killed but left intact. Or the bacterial substances which pass into the media may be separated from the bodies of the organisms and the materials on which they were grown and then injected into the tissues of man to augment his protection against accidental invasion by the same organisms. It is also possible to break up the bacteria and so obtain antigenic substances which were not diffused into the medium. A relatively recent procedure has been devised by which the bacterial antigens can be separated into their constituent haptens and protein components and these fractions then used alone or in new artificial combinations for the purpose of obtaining highly specific reactions against them in man.

These artificial methods of stimulating antibody formation in the human or passively protecting him by preformed antibodies are

[1] Coca, A. F., and Cook, R A Jour Immunol., **8**, 163, 1923.

[2] Dale, H. H.. Jour. Pharm and Exper. Therap , **4**, 167, 1913

[3] Gay, F. P.: Agents of Disease and Host Resistance, Baltimore, Charles C. Thomas, 1935.

[4] Landsteiner, K.: New England Jour. Med , **215**, 1199, 1936.

[5] Weil, R.: Jour. Med. Res , **27**, 497, 1913.

[6] Doerr, R : Ergebn Hyg , **15**, 71, 1922.

[7] Sulzberger, M B., and Mayer, R. L Arch Dermat. and Syph , **24**, 537, 1931.

the basis of all vaccine and serum therapy and preventive immunization. Because they are defensive in nature they will be considered more fully in a later section which deals with the defense against invading organisms.

The *in vitro* antigen-antibody reactions such as agglutination and precipitation are highly germaine to the whole subject under discussion but fall outside of the immediate scope of host-parasite reactions taking place within the host. They are of extreme importance in the study of immunity and have been responsible for most of the advances in the knowledge of the behavior of pathogenic parasites, their genetic relationships, and the vital processes involved in infectious diseases of man and animals. They are also indispensable in specific diagnosis. They are omitted from discussion here because they are more appropriately dealt with in the literature on general and special bacteriology, immunology and diagnostic procedures.

Man's Total Reactivity to Pathogenic Invaders.—The entire man, faced with an invading parasite which is potentially harmful to him, presents a state of possible reactivity to it which is commonly expressed in terms of susceptibility and resistance. The study of this state has revealed that it is invariably reactive in nature, or in other words that man is never passive in his relationship with organisms that invade him either at the time when the invader first comes into intimate association with his tissues or at any period after invasion.

This total reactivity is the result of all of the processes involved in the vital activities of the parasite, the functions of the cells and tissues of the host, and the interactions between the two organisms. It is therefore, the condition or state of the individual at any given moment, represented by his ability to react in a particular way to a particular organism under certain conditions.

The state of total reactivity has been attained as a result of genetic factors in his hereditary make-up, the passive transference of reactive elements or potentialities to him at a time when he as an individual was dependent on his mother, or administered to him subsequent to his birth, and to past experiences with organisms which have invaded him in his prenatal or postnatal existence.

In its broadest terms this total state embraces six recognizable aspects—Susceptibility, Immunity, and Sensitivity and their converses. Within these are included all of the phenomena of invasion, pathogenesis, resistance, and the processes of repair and restoration of function. These latter processes have been reviewed in the preceding chapters; the concern at the moment is with their results.

Susceptibility and Non-susceptibility.—The state of susceptibility is most commonly referred to as the non-immune state but this is incorrect because there are factors which operate to reduce suscepti-

bility which are not concerned with the processes of immunity. As an extreme instance the human is not susceptible to avian malaria but this is not due to immunity.

Susceptibility on the other hand is more than the absence of immunity. It may involve active enhancement by the host of bacterial invasion and pathogenesis. Certain metabolic states and stages of physiologic processes may favor the growth of organisms in spite of immune reactions. It must be admitted, however, that this probably occurs more often after invasion than before although local conditions in the skin and mucous membranes may favor invasion.

If the definition of immunity is confined strictly to that state due to immune bodies, then many of the other defense processes and mechanisms of elimination will operate in favor of or in opposition to invading organisms. A large part of susceptibility would then be due to the weakness or absence of these non-immune defenses.

Susceptibility is frequently a local phenomenon confined to a single tissue or organ or type of cell. Ordinarily this is best observed in the selective action of bacterial products and is the cause of the different manifestations of the specific infectious diseases. If the selective tissues or cells are readily accessible to the processes of organisms brought to the body it will enhance their invasibility. If some bodily condition exists which operates against invasion it will lower the susceptibility of the individual as a whole. This is apt to be of great importance in diseases brought about by organisms which are highly selective in their portals of entry. An attempt to make use of the principle has recently been tried against the virus of poliomyelitis by altering the surface conditions in the nose where the virus is supposed to gain entrance to the nerve terminals.

Immunity and Non-immunity.—At the risk of being too particular immunity will be defined herein as a state of resistance and antagonism toward invading organisms due to particular qualities aroused in the tissues of the host in response to particular qualities possessed by the pathogen. It will always possess the characteristic of vital chemical reactions between the host and the parasite. In contrast to non-susceptibility it ignores those states and conditions brought about by factors not primarily due to the parasite but will admit that these factors may affect the mechanisms of immunity; the two will frequently be found to be functionally interdependent.

The immunity present in an individual is said to be *natural* or *acquired*. These terms are satisfactory only to those who understand their meaning and ignore the connotations in the word natural. The processes and mechanisms by which an individual acquires artificial immunity are just as natural as those included under natural immunity. It is unfortunate that the medical sciences have employed the word natural in a sense different from that of the

other sciences. Colloquially, natural may imply non-artificial but this is hardly scientific usage. Some other word is needed which implies an immunity which results from natural processes not artificially induced.

Topley has more nearly approached the proper use of terms in his classification of immunities into:

1. Innate Immunity.
   (a) Complete.
   (b) Partial.
2. Acquired Immunity.
   (a) Active.
      (a) Naturally acquired.
      (b) Artificially induced.
   (b) Passive.
      (a) Naturally acquired (congenital).
      (b) Artificially induced.

Innate immunity is for the most part a matter of non-susceptibility and not infrequently the result of generic differences, spoken of as Species and Racial Immunity. Furthermore it may possibly be due largely to inborn characteristics which influence the resistance of an individual to infections by the endowment of increased ability to produce the necessary antibodies against specific invaders. This constitutional type of specific immunity is strongly suspected but unproven. The future must differentiate between immune body immunities which are inherent in the individual make-up and false immunities due to metabolic and constitutional differences which create degrees of susceptibility not involved primarily in the strict immunizing mechanisms.

The way in which different diets, animal body temperature, age, sex, and environmental factors account for differences in degree of innate immunity (susceptibility?) has not been determined. Until this can be done it seems wisest to consider innate immunity as non-susceptibility with a willingness to change as soon as any one of the factors mentioned is found to be a part of, or influence directly, the immune processes.

Acquired immunity embraces almost all (if not all) immunity due to antigen-antibody reactions. The individual resistance which depends on this mechanism is then a complex of all of the lesser functions in the process which has been built up from previous experience with a few or many forms of parasite antigens. It is primarily an *experiential immunity*.

The experience with foreign antigens derived from living organisms may have antedated birth and been the result of transmission of the antigens or their corresponding antibodies from the maternal

circulation or tissues. When only the antibodies are received the fetus becomes more or less *passively immune* to organisms of the same antigenic complex as those from which the maternal antibodies were derived. If the antigens themselves pass across or through the placental barrier or are introduced into the fetus by *extension from embryonic tissues which surround it, the fetus may* or may not develop antibodies by the activities of its own immune mechanisms. The infant born under either of these possibilities may therefore be *congenitally immune.*

Active immunity is gained under exposure to infective agents in the environment in the ordinary experiences of existence. In this sense it is a *naturally acquired immunity.* The degree to which a given individual is immune and the number of organisms against which he is immune is determined by the extent of his experience, the degree and intensity of exposure, and all of the non-immunologic factors which participate in the processes by which organisms are favored or antagonized in their attempted invasion. It is here that the part played by the secondary causes can be most clearly seen. They are contributing causes in that they make possible or interfere with the initiation of the strictly immune processes.

In general it can be said that the total acquired immunity is an expression of the opportunities presented to all of the organisms to which an individual has been exposed to force the immunizing potentialities into action and the sum of all individual factors which influence the success of the reactions in the direction of immunity.

The total state of natural immunity is the above plus the passive and innate immunities.

Immunity acquired by artificial methods consists in the exposure of the human tissues to selected antigens or the introduction into the body of antibodies already produced by antigens in other humans or lower animals. In the first instance the antigens call *upon the individual to produce his own antibodies. If the response* is effective it results in *active artificial immunity* against subsequent invasion by organisms bearing the same antigen. When antibodies only are introduced the antigenic stimulus is not present and the immunity mechanisms act for a time to protect the organism against the invasion of infective agents bearing antigens which can produce the same antibodies. The individual so protected possesses *passive artificial immunity.*

In civilized populations today there are many individuals whose total immune state is made up of natural antibodies and artifically induced antibodies present in their tissues and on augmented responsiveness to future experiences with antigens which can stimulate the production of more of the same kinds of antibodies.

This picture is complicated by the presence of sensitivity. In discussing this subject previously it was stated that its exact re-

lationship with the processes of immunity was not yet settled. Nevertheless its presence in an individual under given circumstances has considerable bearing on the immediate outcome of a new exposure to an antigen. The acute reactions of anaphylaxis may be all important to the survival of a person on whom artificial induction of immunity is attempted, and the lesser reactions of an allergic nature can hardly be called insignificant.

Man, the unit of the human herd, may possess complete insusceptibility to a parasite which is pathogenic to other animals or may succumb immediately to an organism even on his first experience with it.

It is this potentiality to react in one way or another which makes up man's total reactivity to parasitic invaders. It is the state of a given individual at any moment under a given set of circumstances.

With this totalitarian view in mind it is possible to understand the degrees of success which an invading parasite obtains as measured by the outcome to the individual.

Complete insusceptibility or complete immunity to any given parasite will mean that neither disease nor death can occur. In the absence of complete insusceptibility the outcome will be the resultant of the degree of susceptibility and the amount of immunity present against the particular organisms of a given strain or type and virulence. When susceptibility is high and immunity low or absent death may readily ensue. If, however, susceptibility of any degree is admitted the result will be determined almost entirely by the amount of immunity. A high immunity may permit the organisms to survive for a long period of time as a latent infection without the formation of local lesions but as the amount of immunity is lessened the greater will be the probability that the organisms can gain a satisfactory foothold and set up local lesions or go on to systemic invasion and death. (The conception on which the above account is based is shown in graphic form in Topley's "Outline of Immunity," London, Edward Arnold, 1933.)

The infected individual may reveal evidences of the invasion by clinical manifestations of the disease or he may present all of the outward aspects of good health. The latter is especially true in *latent infections*. The use of this term has come into use in medical literature before it has been possible to define it with accuracy. It implies invasion by some pathogen but the resulting pathogenesis may not be demonstrable by the ordinary clinical procedures; the determination of its presence is usually indicated by special studies intended to reveal the presence or absence of serologic changes brought about by the specific agent.

The *carrier state* is looked upon as a host parasite relationship in which the infective agent is not at the moment responsible for any existing pathologic processes. The organism may be *on* the body,

but it has not invaded its tissues or it may be *in* the body and kept in complete abeyance by protective mechanisms. In the first instance the individual may never have been the subject of the disease which the organism he carries can produce. Such for example are the healthy carriers of meningococci and pneumococci in their naso-pharynx but who have never had epidemic meningitis or lobar (diplococcal) pneumonia. The second consideration would be met by one who has had a specific infectious disease, the pathology of which has entirely cleared up, but who still harbors the organism in a *harmless state of balance with the defense mechanisms of the body*. The obvious difficulty in making an actual distinction between latent infection and the carrier state is the difficulty of establishing the presence or absence of current pathology. This is complicated *still further by the possibility that a carrier may* at any moment become invaded by the organism he is carrying and that the course of a latent infection may be frustrated and the host-parasite relationship sink (or rise) to the carrier state.

Furthermore, the total reactivity of an individual is not static. Since the total state is a complex of immune and non-immune processes which combine to make him more or less invasible by a given organism any influences which act to strengthen or weaken the elements on which his resistive state rests will tend to disturb his equilibrium.

Among the factors suspected of influencing the total state are: dietary defects and indiscretions; poisonings by such generally acting substances as alcohol; metabolic and physiologic changes accompanying puberty and adolescence, pregnancy, fatigue and exhaustion; intercurrent disease; and environmental changes in the meteorologic complex. These are matters of common observation which bear a high degree of statistical correlation with changing states of health, but unfortunately correlation is not proof. A scientific explanation for the effects produced by these factors is not yet at hand for any one of them.

In summary it can be said that the individual faced with an invading organism will react at any moment in a way dictated by the past experience with that organism by either his race, his parents, or himself and possibly also to a degree determined by his immediate physiologic state and external environment. Because he is plastic in his reactions an understanding of his activity as a unit of a herd is essential to the interpretation of the phenomena of the herd of which he is a part.

Phenomena of the Infected Herd.—When an organism which is capable of invading man exists in a human community it will tend to invade some of the members of that community according to whether conditions exist which favor or operate against its approach and acquisition by the human members, and the state of reactivity

of the latter toward it and subject to the invasive powers of the organism itself. The probability of the survival of the organism in the community will then depend on the net result of the above equilibrium and the degree of importance of man as its obligate host. Could all of these factors be known the outcome of an experience of a given organism in a given herd could be predicted. Unfortunately this is impractical because neither the herd nor its units are static and there is a strong probability that the invasibility of the organism, from its own biological aspects, is also variable.

There remain sufficient data, however, on which fairly definite judgments can be made. This is especially true in the instances of those organisms in which immunity reactions play a relatively small rôle against them, and their attack rate on man is largely dependent on opportunities for their acquisition by man. The extremes may be represented by the difficulty of predicting the outcome of an invasion by the virus of poliomyelitis or the diphtheria bacillus on the one hand, or the far more simple problem of the hookworm or the tapeworm on the other.

Among many of the bacterial diseases immunity undoubtedly plays such an important part as to justify the application of the expression *Herd Immunity* to the major manifestation of the host-parasite milieu. In these diseases transmission of the parasite from host to host is relatively direct (except in the case of those dependent on insect transmission) and it can be assumed that all members of the herd are about equally exposed or have equal opportunities of exposure. Also, the variability of the organisms appears at present to be of relatively little importance. Furthermore the majority of individuals are equally subject to all important environmental factors. This leaves individual susceptibility and resistance as the outstanding influences that determine success or failure for the parasite.

Topley (Outline of Immunity, 1933) lists six states in which the members of the herd exist in relation to past experiences with a given parasite (1) the typical case, (2) the atypical case, (3) the latent infected, (4) the healthy carrier, (5) the uninfected immune, and (6) the uninfected susceptible. Each of these represents a state of total reactivity toward the organism either in the direction of resistance or away from it. It can also be assumed that in 3 and 4 there are no outward manifestations of the disease and these individuals will be observed as apparently healthy members of the community along with 5 and 6. It was the demonstration of this which brought enlightenment to the study of epidemiology. As long as superficial observation by bed-side studies formed the only criteria on which to base the prevalence of an infective organism in a community the reservoir of the infection was looked for in every place except where it actually existed.

Healthy carriers and cases of latent infection are generally in the position to be unsuspected disseminators by virtue of their freedom to move about in the population and because they themselves may not be aware of their potential danger to others.

Endemicity and epidemicity of an infectious bacterial disease are best understood by reference to the proportion of each of the above groups in the herd. If all are uninfected immunes and no new susceptibles are admitted to the herd no disease can develop. If all are uninfected susceptibles an organism introduced into the community may devastate the herd if the organism possesses severe enough virulence to produce one hundred percent fatality. Practically a new bacterium brought into a virgin society does not carry such disastrous potentialities and some members attacked recover from the disease. Those who pass safely through the experience may then be left free of organisms and immune, or as healthy carriers, or latently infected. The community now settles down to an equilibrium with the organism which is manifested by the sporadic appearance of typical and atypical cases among those who have lost all or part of their immunity respectively, and occasionally, as more and more of them become less and less immune and new recruits are added to the colony by birth and immigration, a sufficient number of susceptibles appear to permit a widespread invasion by the bacterium as an epidemic with large numbers of typical cases. But even then some susceptibles do not succumb to the infection because of the operation of other factors and they only pick up the organisms and become healthy carriers.

The actual outbreak of an epidemic is dependent therefore on the perpetuation of the organism in the community in infected individuals and its transmission almost simultaneously or in rapid succession to large numbers of susceptibles. The occasion and opportunity for this spread is probably supplied by environmental factors which may affect the biologic activities of the organism or the reactivity of the hosts or both, or in some way favor the survival of the bacterium between hosts and enhance its accessibility to them. The actual dose of organisms per host may prove to be an important factor in many instances. Mention must be made again of the possible rôle of dietary factors, age increase, and concurrent diseases which may influence the reactivity of the herd as a whole against a particular invader.

Artificial immunization of susceptibles should act to keep down the possibilities of an epidemic but the actual fact of its effectiveness in human populations has not been definitely determined. While this wholesale immunization is proceeding it is not unlikely that the carrier rate is increasing and it is obvious that the inability to control immunization completely might ultimately make the herd more widely infectious than before. Unfortunately immunization

sufficient to prevent disease is not equally effective in preventing the carrier state and therefore untempered optimism toward the ultimate goal of wholesale immunization and eradication of a given disease is not warranted at present.

In diseases like yellow fever, malaria and the trypanosomiases where the organisms exist entirely within their human and animal hosts the major determining influence on their continuance in a community is the ecologic status of the lesser host. If the host survives in large numbers and has been successfully infected by the organism in question the incidence rate of the particular disease in a community will be high. Also the periodicity of increases in the attack rate will be determined largely by factors which influence the animal host more than they do the parasite it contains. The seasonal prevalence of malaria is almost wholly dependent on such a factor.

A complication may appear in the above picture when a reservoir host is added. In such an instance man becomes of relatively less importance but he cannot expect to eradicate the disease from his community so long as the lower animal-reservoir relationship remains undisturbed. Although mild degrees of immunity may have a slight effect on the susceptibility of the human hosts in these diseases practically it is too mild to have very great significance for the herd. Infection immunity, as is believed to be the case in malaria, may be highly influential in keeping down large epidemics. Increases to epidemic proportions in malaria are believed to be largely due to exceptionally favorable environmental conditions which increase the mosquito population and therefore the mass infection rate of this indispensable disseminator of the parasite.

Helminth and protozoan infection in a herd depends so largely on the opportunities offered for the propagation and dissemination of the parasite that the case rate is usually dependent on one or more relatively simple associations between the parasite and its environment. These have been rather fully reviewed in previous chapters to which the reader is referred. A complete account of the loci of each organism in the environment of man is given in an alphabetical list of the human pathogenic parasites beginning on page 395.

For detailed studies of mouse populations infected with organisms under controlled conditions reference is made to the publications of Greenwood and Topley,[1] Greenwood, Newbold, Topley and Wilson,[2] Greenwood, Topley and Wilson,[3] and Marchal.[4]

[1] Greenwood, M., and Topley, W. W. C.: Jour. Hyg., 24, 45, 1925.

[2] Greenwood, M., Newbold, E. M., Topley, W. W. C., and Wilson, J.: Jour. Hyg., 25, 336, 1926; Ibid., 28, 127, 1928.

[3] Greenwood, M., Topley, W. W. C., and Wilson, J.: Jour. Hyg., 31, 257, 1931; Ibid., p. 403; Ibid., p. 484.

[4] Marchal, J.: Jour. Path. and Bacteriol., 33, 713, 1930.

CHAPTER XLIV.

THE DEFENSE AGAINST INVADING ORGANISMS.

MAN is safe from the pathogenic parasites only insofar as he can avoid their ultimate invasion of his tissues. But since he is constantly circulating through the environment in which the parasites exist and they in turn are in active motion or are passively transported from place to place in the same environment it is impossible for him to avoid countless opportunities for parasitic invasion. The fact that many of the parasites depend on man for their survival, and that man lives with man, multiplies the probability of chance invasion many fold.

The problem of the prevention of infectious and parasitic diseases is therefore as wide as the environment in which man moves and the organisms exist, and as narrow as the immediate portals of entry of the individual who is subject to invasion.

The individual may take up his own defense against invaders. Under these circumstances he is acting independently on his own behalf. Or he may act for others socially dependent on him who voluntarily submit to his judgments and regulations. But even this autocratic individual is not permitted complete individuality. He is a member of society by virtue of biologic, social and economic demands that make it necessary for him to live with others of his kind. This demand for social living creates a responsibility on the part of society toward its own welfare and that of its members, and its earliest concerns therefore must be the health of the herd and its member units.

The combination of individual responsibility and social solicitude makes up the total human attitude toward the defense against harmful living organisms in the environment. Out of the individuality must grow all efforts to stimulate the members of society to contribute their share toward the control of infection and parasitism in themselves and others, and from the social responsibility and solicitude must come the intelligent approach toward the maintenance of the health of the herd, as expressed today in the functions of Public Health.

The mechanisms for the prevention and control of diseases caused by living agents in the socio-environmental complex must act in such a way as to cut across the paths of the disease agents wherever they exist—they will necessarily operate on and around the members of the community, in every group and organization, at every point where the agents live, multiply and spread, and at the peri-

phery of the organized community where the parasites may gain admission to it. The whole effort can be visualized as a spiral whose outermost circuit embraces the whole community and the ever diminishing turns cut through the society in narrowing circles until the final twist involves the individual at the center. The outer circle will represent the blanket measures thrown about the community for its protection from outside invaders, the lessening circles of the spiral will cut across the processes which favor the existence and spread of the organisms, and the central focal point will be those mechanisms evolved to protect the individual from immediate invasion.

In the ensuing discussion the concept of organization will be maintained irrespective of whether the organized body be made up of few or many members. It will also be independent of the degree of organization provided only that it has a relative permanence. In this sense an organization of human units may be a family, village, town, city, state or nation. Explicit social organization may be barely recognizable or as complex as the systems of a highly organized state. The fundamental interests of all are the same and the same natural laws apply to each. The growth of a central authority will be understood to be a necessary development as the complexity of the organization increases. Insofar as this authority is vested with the duty of safeguarding the health of the herd it will be called the Public Health Authority. The terms *community* and *society* will be used interchangeably with *social organization.*

PROTECTION BY PURIFICATION OF THE WATER SUPPLY.

Among the primary interests of every social organization is the maintenance of its water supply. Where the concern was formerly only with the quantity of water, it now demands that it be qualitatively pure. This has grown out of the knowledge that water is a potential bearer of many infective agents. A study of the sources of contamination, together with knowledge of the types of organisms carried by water, permits the application of effective measures which will prevent contamination of the supply and destroy or remove such harmful living disease agents as might already have gained access to it.

The smaller the social unit the more individual will be its water supply. In rural areas this is most frequently the homestead with its stream, spring, well, or cistern. All of these sources can be readily contaminated the most common coming from circumstances which permit the entrance of human and animal excreta. A stream, by its very nature, is lower than the ground about it and continually receives the ground water seeping through its banks and the surface

water which runs off after a rain or is thrown onto the ground around the dwellings. In this way feces and urine which contain pathogenic organisms are readily washed into the water supply. Because of their constant flow away from the source of contamination, streams are likely to be more dangerous sources of water for those living down-stream than for those who contaminate them.

Surface springs and wells become contaminated in the same way but because the water in them is relatively still there is more opportunity for a higher concentration of the contaminating material. Unless there are definite faults in the earth about deep springs and wells it is doubtful if many organisms can gain entrance by way of the soil except through the upper foot or more of ground. If deep earth wall privies and cess-pools are near a spring or well they may penetrate the same porous layer and permit the seepage of contaminating materials into the water supply. Wells drawn by a pump may have their water level so lowered as to create a new flow of ground water toward them and thus add to the possibilities of contamination. In springs and wells in which there is little or no surface overflow refuse and foreign matter may fall in and remain floating on the surface or in suspension, or settle to the bottom. Deep wells which give an otherwise pure supply of water may be contaminated by faulty construction at the ground levels or leaks and breaks which result from wear and tear of pumps, windlasses, etc. Even artesian wells can be made unsafe by rust holes, cracks, and faults occurring in the region of the upper ground water or at the surface level.

Cisterns are filled by rain water which falls on collecting surfaces, usually roofs and gutters. The water washed into them will be only as clean as the rain itself plus dust and débris which has accumulated on the collecting surface and drains between showers. However, pathogenic organisms in falling rain can be ignored, and those on roofs and gutters are practically negligible. If the collecting surface is on the ground it is much more open to contamination. The secondary contamination of the water in the cistern, if it is underground, is the same as for springs and wells.

All of the above sources can be further contaminated by the introduction of dirty dippers, buckets and siphons used to draw the water.

Prevention of contamination of these small unit water sources resolves itself into two main considerations: (1) the location of the supply in respect to sources of contamination; (2) the proper construction of artificial retaining walls, covers, and water-drawing devices.

If there is any alternative in the selection of a natural spring, one should be chosen which is away from the direction of flow of the ground and surface water coming from nearby dwellings, out-

houses, barns, animal pens and privies. It must be remembered, however, that such a spring if artificially deepened may invade a porous layer underlying the dwelling and its compound even though there may be a rise of ground between them. Unless the spring is on a higher level than the surrounding property and has no other inhabited grounds on a hill above it, positive assurance of a pure, uncontaminated supply cannot be had unless the spring is protected by artificial means.

The spring and surface well, and the surface parts of deep wells and artesian wells, should be enclosed with masonry. Brick and mortar casing, pointed on the inside and tamped on the outside with clay or cement, should extend not less than 1½ to 2 feet above the ground level and as deep below the surface as may be practical without shutting off the springs. A solidly constructed platform or sill should surround the coping of the well and extend from it for a distance of 3 or 4 feet. The surface of the sill should be waterproofed by cement or closely caulked boards; it should be tightly joined to the coping. The discharge pipe from the pump or overflow from the spring should extend beyond the outer limits of the sill and be directed in such a way as to carry the waste water toward some natural or artificial ditch, drain or other water-way. The need for a cover over a spring or well must be left to the particular circumstances in the case.

Larger communities frequently resort to a common source of water from a river, lake, pond or reservoir. The larger the community and the greater the demand for a constant supply of water the more commonly will combinations of natural and artificially impounded water be required. It can be taken for granted that natural bodies of water in the immediate vicinity of large communities is contaminated. Streams and rivers are supplied by water coming from their tributaries and flowing off of their banks from the neighboring hills and valley lands. Many of these areas are inhabited by humans or occupied by live stock and other animals, and are common sources of contamination.

Whether the water supply is drawn from the river and used directly or is impounded temporarily in reservoirs it is likely to be contaminated. Contamination in the reservoir can be reduced if the water is allowed to stand for three or more weeks because standing favors sedimentation and the time element allows the natural destruction and death of pathogenic organisms.

Lakes and ponds are equally liable to contamination but they may be safer than a stream or river because they act as natural reservoirs. However, if contamination is high they cannot readily sterilize themselves and are then dangerous water sources. Large lakes are *ipso facto* safer because of the higher dilution of contaminating materials which enter along the shore lines. Currents

in large lakes may be the determinating factors in the location of sewage outflows and water intake pipes.

Artificial reservoirs fed from catchment areas can *only* be *free* of contamination if the surface of the areas is uncontaminated. Otherwise they are as potentially dangerous as natural lakes.

Where authority exists to enforce them laws should be enacted to prevent contamination of public water sources. *The community* may own and patrol the water sheds of its source streams and catchment areas, and regulate the use of the lands adjoining reservoirs. Individual ordinances to fit particular cases are usually necessary.

The engineering problems involved in the construction of dams and reservoirs and the specifications for materials, equipment, and machinery used to pump and distribute the water are beyond the *scope of this book.*

On the assumption that all public water sources are probably contaminated every community should subject its water supply to some form of purification before it is used. For the purpose of *determining the effectiveness of any system of purification* a bacterial examination of the water can be made before and after treatment. This consists of the bacterial count of the total number of organisms per cubic centimeter of water after twenty-four hours' *growth on standard agar plates at 37° C., or the determination* of the presence of bacteria of the *Escherichia coli* group alone. In the United States, the official government standard established in 1925, refers to the percentage contamination with *E. coli* of standard volumes of water. The water after purification must meet this standard to be certified as fit for human consumption. The following are the specifications for the standard purity of water (as to bacterial content) in public water supplies in this country:

"1. Of all the standard (10 cc.) *portions* examined in accordance with the procedure specified, not more than 10 percent shall show the presence of organisms of the *E. coli* group.

"2. Occasionally three or more of the five equal (10 cc.) *portions* constituting a single standard *sample* may show the presence of *E. coli*. This shall not be allowable if it occurs in more than

(*a*) 5 per cent of the standard samples when 20 or more samples have been examined.

(*b*) One standard sample when less than 20 samples have been examined.

Note: It is to be understood that in the examination of any water supply the series of samples must conform to *both* the above requirements, (1) and (2).

"The *standard portion* of water for this test shall be 10 cc.

"The *standard sample* for this test shall consist of 5 *standard portions* of 10 cc. each."

The bacterial content of water in bulk can be reduced by storage, sedimentation, coagulation, filtration and chemical treatment.

Storage in reservoirs permits the suspended particles in the water to settle to the bottom and carry bacteria with them. It also provides the opportunity for protozoa to ingest bacteria. Most of the pathogenic organisms cannot survive in stored water for more than a few weeks so storage should be continued for at least three weeks or a month. The prolonged exposure of a large surface of water to sunlight is also detrimental to bacteria and many organisms are destroyed by the natural oxidation processes which take place. Storage is one of the most economical processes for the reduction of gross contamination after the initial expenses of construction have been met.

Sedimentation is resorted to primarily for the purpose of reducing a heavy content of suspended particles but bacteria are also reduced at the same time. Because the time required for clearance of sediment is much shorter than that necessary for effective reduction of the bacterial content, it should not be relied upon for purification unless it is combined with the principles of storage.

Coagulation depends on the addition of alum to water in such proportions that all of the alum unites with the natural alkalies to form aluminum hydroxide, a heavy colloid which quickly settles and carries suspended matters with it. The bacteria in suspension are not destroyed in the process but are mechanically removed from all but the bottom layers. For this reason coagulation is used only as a preliminary to some further method of purification.

Alum is added in the proportion of about 3 grains to 1 gallon of water. The actual amount in each case must be determined by the pH of the water in order that sufficient alum may be added for the purpose in view and that there should not be more alum than can be combined with the alkalies. The time allowed for the flocculant to precipitate may be from a few hours to a few days depending on the amount of sediment and the method of purification to be used later.

Sulphate of lime and iron combinations are also used to form a chemical precipitate of iron hydroxide on the same principle as above. The exact amounts of ferrous sulphate and lime to be added must be carefully controlled by continued re-examination of the pH of the water. The ferrous sulphate is used in the amount of about 1 grain per gallon (17.1 parts per 1,000,000) and the lime to be added for the necessary chemical reaction approximates 0.2 grains per gallon (28.6 pounds per 1,000,000 gallons).

Filtration of large amounts of stored water is accomplished by causing it to pass through layers of inert gravel and sand filters. The sand *per se* has no direct bacterial effect and is in that sense inert, but it is not to be deduced from this that the action of sand

filters is entirely mechanical. On the contrary the total action of a filter is a combination of mechanical interference with the passage of suspended particles through the interstices of the filter, the phenomenon of adsorption, and the biologic activities of the restrained organisms as they accumulate in living masses with other organic and inorganic materials on and in the upper layers of the filter bed. The net result is the formation of a zoögleal mass representing living organisms and organic slime. In this growth most of the pathogenic bacteria succumb.

While all such filters depend on sand they vary in their porosity and depth. The rate of flow through them is determined therefore by these mechanical factors. A *slow filter* is one composed of a layer of sand, selected for its uniformity in size of grains, 3 to 4 feet thick and resting on an 18-inch layer of graded gravel. Beneath the gravel are open tile drains which carry off the filtered effluent. The amount of water which can be filtered through such a system with a vertical flow of 3.28 inches per hour is about 4,000,000 gallons per acre per day. Since it is the upper few inches which collect most of the foreign matter the hour required to pass through these 3 inches is of great importance because it permits time for the biologic processes to exert their greatest effect.

For the technicalities of construction and operation of slow filters the reader is referred to standard works on the engineering aspects of filtration systems.

Rapid sand filters depend more largely on the mechanical removal of suspended particles. This is possible because the water has first been subjected to sedimentation and coagulation before being brought to the filter beds. The coagulum accumulates on the surface of a layer of relatively coarse sand some 2 to 3 feet deep overlying 12 to 18 inches of graded gravel. The head pressure due to gravity is sometimes increased by adding some compression device. Rapid filters can pass 100,000,000 to 175,000,000 gallons per acre per day. There is little time allowed for the development of a biologic zooglea on the sand but in its place there develops an artificial *schmutzdecke* made up of the alum or iron-lime coagulum resulting from the preliminary treatment in the sedimentation basins.

Rapid sand filters are also called mechanical filters because some mechanism is installed which will reverse the flow of water through the filter for the purpose of cleaning it. This is in contrast to the removal of a few inches of sand at a time from the surface of the slow filters as they lose head pressure from clogging of the pores.

Slow sand filters under proper operation remove 98 to 99 per cent of suspended bacteria and rapid sand filters from 95 to 99 per cent. In both instances all pathogenic organisms and almost all *E. coli* are removed so that the filtered effluent should conform to the water purification standards in America.

Additional safety in the water-supply to a community can be obtained by *chemical treatment.* The chemical substances most commonly used against bacteria are ozone, chlorine, ammonia-chlorine, silver, potassium permanganate, and copper sulphate.

Ozone acts as an oxidizer on the organic materials in water and is an effective bactericide. The ozone, produced from air in an electric discharge ozonizer, is passed upward through a tower in which filtered water is entering slowly at the top and trickling down to a reservoir at the bottom. Clear filtered water requires from 1 to 3 milligrams of ozone per liter of water for purification.

Chlorination may be obtained by the use of chlorinated lime, liquid chlorine, chlorine gas, or chlorine in combination with ammonia. In each instance the bactericidal effect is due to the action of nascent, unhydrolyzed chlorine. Chlorinated lime in water undergoes chemical reactions resulting in the formation of calcium hypochlorite and hypochlorous acid along with other intermediate products. The hypochlorous acid is unstable and reacts with other hydrogen and chlorine ions to form chlorine and water. Chlorine or chlorinated lime and ammonia in solution in water produce potently bactericidal chloramines.

The amount of the various forms of chlorine to be used are usually expressed in terms of available chlorine. One part of chlorine per 1,000,000 parts of water is obtained from 26 pounds of chlorinated lime per 1,000,000 gallons of water. The average amounts used in terms of chlorine range from 1 to 4 parts per 1,000,000. The variability depends on the amount of organic material in the water. Since some of the chlorine is used up in the oxidation and bleaching of these organic substances there is less available for the destruction of bacteria. The waters containing the most organic matters therefore require the larger amounts of chlorinating substances.

One part of chlorine per 1,000,000 parts of water is obtained by adding 8.3 pounds to 1,000,000 gallons of water.

The ammonia-chlorine combination is most readily and economically obtained by the use of liquid chlorine and ammonia.

Metallic silver appears to possess a catalytic action in water which is bactericidal in minute amounts. A thin silver coating is placed on grains of sand and the sand is then added to the water. The silver passes into the water and exerts its bactericidal effect presumably by catalytic activity in conjunction with oxygen. The silver preparation is called "Katadyn." It is only active in clarified waters which contain no suspended impurities and it requires several hours for a complete sterilizing effect.

Potassium permanganate is an oxidizing agent and its bactericidal power depends on this property. In the proportion of 0.5 parts per 100,000 of water it reaches its maximum bactericidal effect in from

four to six hours. It has been shown that higher concentrations for longer periods of time are no more effective. For large scale use it is expensive and inferior to the chlorination methods but it finds its greatest usefulness as an emergency measure in the sterilization of contaminated wells and pools. It may remove 98 per cent or more of bacteria when used in the above proportions but this cannot be relied upon because its effectiveness is greatly reduced by the presence of organic matter.

Copper sulphate in proportions of 0.1 to 0.25 parts per 1,000,000 parts of water is destructive to algæ and other microörganisms in this dilution but does not destroy many of the important members of the intestinal group of bacteria. It has qualities, however, which are useful in the preparation of esthetically potable waters but this is not pertinent to the present discussion.

The administration and technical direction of these large-scale purification methods requires a highly trained personnel and sufficient authority to act as freely on its own accord as is compatable with the organization of the community it is set up to protect. But because the health of the community may be seriously jeopardized by the failure for any reason of the system of water purification on which it relies, the controlling authority must operate under rigid standards of efficiency. When both of these necessities have been met the water authority will be flexible enough to meet all contingencies and yet maintain its standards without the embarrassment of time-consuming ineffectual interference from without.

The central water supply system is therefore an example of an efficient blanket protective measure. It does not aim to restrain or destroy specific living disease agents but is so constituted as to exclude *all* living pathogens which may be expected to enter the community from that source.

In a community which has not the assurance of a safe water supply, either from a central water purification plant or individual sources which are above reproach, resort must be had to methods of purification *after* the water has been drawn from its source. Such conditions exist in rural areas where sanitary methods are not known or not practiced, and in remote regions where no opportunity exists to safeguard the purity of the water source. Armies in camp or on the march are faced with similar circumstances. In small villages or towns economic factors may prohibit the expense of special provisions for a clean water supply. In still other areas local conditions and habits of the people may be such as to preclude any possibility of maintaining the purity of the water during its distribution to the consumer.

In each instance the responsibility for providing uncontaminated water for consumption and culinary purposes must rest on the unit

which is going to use it, whether it be a public or private institution, an army unit, a camp, a household or an individual.

Institutions such as factories, sanitaria, jails and hospitals in outlying districts should be safeguarded by artesian wells or other irreproachable sources of their general water supply but they should be prepared for emergencies created by breakdown or contamination of the general water supply. This means that they should be prepared to use other sources on short notice or to treat the ordinary source to render it safe. The latter can best be accomplished by chemical disinfection or boiling.

Water is effectively sterilized by boiling for fifteen or twenty minutes. This may be accomplished in institutions by the use of boilers of many gallons capacity or in the household in any satisfactory pot.

Emergency chemical disinfection can be obtained by the use of any of the chemicals discussed in the previous section. For immediate use in small installations chlorinated lime is the most practical. It can be made up in concentrated solution in the proportion of 1 teaspoonful of chlorinated lime to 1 pint of water. For use, 1 teaspoonful of this solution will be sufficient to disinfect 10 gallons of water in fifteen to thirty minutes. The chlorinated lime must be fresh.

Commercially prepared tablets of hypochlorite, and chloramine may be added in accordance with instructions.

Ozonizers are employed in some institutions which rely on an independent water supply.

The sources of secondary contamination of an otherwise satisfactory water supply are from defects in the distribution system, contamination during temporary storage, or the admission of infected organisms by unsanitary handling during the use of the water.

Distributing pipes from the purification plant may develop faults, leaks and breaks by chemical erosion or the mechanical effects of explosions, digging operations, earthquakes, floods, unskilled repair work and faulty connections between water supply pipes and the sewage disposal system. A more serious contamination can occur with a break-down or fault in the central supply plant.

The ultimate effect of any of these causes is to place the community in the same position as one which has no central protection and those depending on it must resort to individual methods of purification.

Large institutions not infrequently have their own storage tanks and cisterns for economic or other reasons. If they are faultily located or badly constructed they may become contaminated by effluvia from septic tanks, toilet discharges and factory wastes.

All of the above should have the protection of frequent and

efficient inspection. The community regulations should provide for control over the installation of all public systems and the inspection and certification of plants in private institutions.

In the home and in army and labor camps and in small social units such as villages, motor camps, and private institutions the water is commonly collected in storage tanks, cisterns, tank cars, water coolers, and various forms of makeshift containers.

The frequent lack of foresight in the placement of these storage facilities in the neighborhood of privies, cesspools, camp disposal heaps and so forth, is a patent disregard of the very principles of water sanitation. Those responsible for them often have no understanding of the precautions to be taken in storing water and less knowledge of the proper construction of the containers. That they must be water-tight is the only obvious specification with which they are acquainted. But beyond this they should be well covered to prevent infected materials from falling into them, they should be accessible to thorough and frequent cleaning, they should be protected from back-splashing when water is being taken out by hand methods and where pipes are used all connections should be tight and faultless.

Contamination of the purest water supply may occur at the time it is being used and vitiate the whole effect of an expensive, efficient plant, or for the individual householder, may make useless all of the care and intelligence he may have put into the protection of his independent supply.

Dirty fingers are the greatest single source of such contamination. Food handlers, cooks, housewives, water-boys, waiters, etc., who are unwittingly careless in their personal hygiene may inject dangerous organisms into a bucket or glass of water with a single dip of their fingers in it. More gross contamination can occur by repeated dippings with a common drinking cup or dipper into a bucket or the dropping of infective materials into it from a human or animal source.

For these reasons common drinking cups should be interdicted in public places and all containers should be protected by effective covers to keep out contaminated particles. Drinking fountains of acceptable design should be the only sources of public drinking water.

The community control of public food handlers will be considered later.

In the private household secondary contamination means unclean habits. Water standing around in all sorts of containers for the common use of all who will, in any way they may feel disposed, permits easy contamination from fingers, lips, saliva, discharges from open sores and even human excrement. These factors will be discussed under personal hygiene in another place.

All measures taken to insure the maintenance of the purity of water after it has been rendered safe at its source are general preventive measures. Although they aim to reduce infection due to all forms of organisms they protect a relatively smaller number of individuals than the blanket community measures. They are therefore intra-community, and are applied at those points in the spread of infective agents in the environment at which the organisms become vulnerable. If the efforts at prevention at this stage are complete their effectiveness so far as the individuals are concerned is as absolute as the measures taken to keep the organisms out of the community entirely. Unfortunately the human element plays so great a part that they cannot be relied upon to too great an extent. For this reason they should not supplant the broader plan of central purification but should supplement it at all times and especially during emergencies.

PROTECTION BY CONTROL OF THE MILK SUPPLY.

Urban communities are generally dependent for their milk supply on sources outside of their political limits. In their own interests they are concerned with the quality of milk to be distributed to their members because of the recognition that a number of important pathogenic organisms are transmissible by milk. Unless the milk-producing area around the community is under the control of a larger social unit such as a county, parish, state, province or national organization the smaller community can assure itself of a pure milk supply only by setting up rigid standards of quality for all milk entering its borders. The same principle will also apply to larger social units which receive some of their milk from outside sources. Because the jurisdiction of a political unit does not extend beyond its borders it can have nothing to say about the purity of the source of the milk other than through indirect methods such as economic and political pressure. These are so potent, however, that they can be extremely effective if wisely applied.

Every community should establish definite standards for milk and enact such ordinances or laws as are necessary to enforce them. In the United States it is customary for organized community medical associations to establish standards through a Medical Milk Commission appointed from its members. This Commission then examines, or has examined, the milk from all sources and certifies it according to its standards. The Commission has not the authority of law but its judgments exert strong economic pressure on the milk dealers and may act as a basis for the formulation of controlling laws.

As unreasonable as it may seem, all milk sold is ordinarily not required to come up to a single standard of bacteriologic purity. In most areas raw milk is allowed, but if it is to be certified by the

Medical Milk Commission it must meet the Commission Certified Milk Standard. Certified milk may also be pasteurized, but this is optional. Grade A and Grade B milk are pasteurized milks dispensed under less exacting requirements than certified milk.

The essential requirement of clean milk is that it must not contain pathogenic organisms and be relatively low in the content of all other forms of bacteria.

The extent of bacterial contamination of milk is determined by plating measured amounts of milk on culture media in Petri dishes. *After incubation the number of bacteria is estimated by various* counting procedures and the number calculated per cubic centimeter. A rough estimate can be made by determining the length of time the reductase in milk containing bacteria will take to render colorless a standard solution of methylene blue. The interpreta*tion of the test gives a rough index of the contamination and age of* the milk. Good milk requires about five and one-half hours to decolorize methylene blue, fair milk from two and one-half to five hours, bad milk twenty minutes to two hours and very bad milk less than twenty minutes. This is a convenient test for crude *sampling on farms and at collecting platforms.*

Certified milk is a raw milk produced and distributed under a contract between the dairy and the Commission. The contract specifies that the milk shall not contain more than 10,000 bacteria per cubic centimeter, must not be more than thirty to thirty-six hours old at the time of delivery, that the milk and the dairy are open to periodic inspection and that the cows are certified by a veterinarian as being tuberculosis and abortus free as determined by the tuberculin test and other examinations. It also requires *that the milk shall be obtained under sanitary conditions in the* dairy and shall be placed immediately in closed containers at a temperature not exceeding 45° F. and that it be kept below this temperature until delivered.

Grade A raw milk must meet the same bacteriologic requirements as Certified milk but the conditions under which it is produced are less exacting.

All other milks admitted to a community should be rendered harmless by pasteurization. The quality of the milk can be determined from time to time by the bacteriologic examination of random samples taken from distribution agencies.

No admitted milks should contain any pathogenic organisms. *Grade A pasteurized milk* must not contain more than 200,000 bacteria per cubic centimeter before pasteurization and not more *than 10,000 per cubic centimeter after pasteurization at the time of* delivery to the consumer.

Grade B milk is always a pasteurized product. It may have contained as many as 500,000 bacteria per cubic centimeter before

pasteurization but must not show more than 25,000 per cubic centimeter when delivered to the consumer.

Certified milk may also be pasteurized and approved by the Medical Milk Commission as Certified Pasteurized Milk. This will give the purest milk available and is a standard highly to be desired.

Tinned condensed and evaporated milks and milk powders are rarely any problem for the sanitary control bodies of a community because they are well sterilized by the processes under which they have been prepared. Condensed milk may not be entirely sterile if it was made from an unclean milk because its thickness may prevent the penetration of heat to all parts.

Dairy products such as cream, butter, soured milks, ice-cream and cheese are likely to be only as free of organisms as the raw milk from which they were made. For this reason only pasteurized milk should be used in their manufacture.

Milk produced and distributed within a community is readily brought under legal control in every respect.

In the first place the cow or goat source should be registered and examined by qualified veterinarians and only sound animals be permitted to produce milk for human consumption. The two most important diseases of sanitary importance to which these animals are subject are tuberculosis and contagious abortion.

Only cows showing negative tuberculin tests should be permitted to produce market milks. All reactors should be disposed of by killing or by isolation under the Bang system. The latter would permit the separation of reactors from the tuberculosis-free herd for the purpose of calving but the calves must not nurse from the infected mother. They may, however, drink their mother's milk after pasteurization. The tuberculin test on cattle should be repeated at not less than yearly intervals.

All cows or goats which show clinical evidence of contagious abortion or reveal infection with *Brucella abortus* or *B. melitensis* should be destroyed.

The milk ducts, teats and udders of cows always contain some bacteria among which may be such pathogenic organisms as streptococci (hemolytic and epidemicus varieties), diphtheria bacilli, organisms of the dysentery group, foot-and-mouth disease virus and typhoid bacilli. Although it is impossible to sterilize the teats and udder the bacterial contamination can be markedly reduced by thorough washing with clean water and the use of hypochlorite solution. If all other precautions are equally carried out a fresh raw milk can be obtained directly from the cow with a bacterial count of less than 10,000 per cubic centimeter.

The unattended cow must be considered as a filthy animal. Its hind parts and belly are always dirtied with manure. To render

it as cleanly as possible it must be thoroughly hosed down, curried and scrubbed.

The sanitation of the milking stalls is not difficult to attain if the flooring is of cement with adequate free-flowing drains behind the cows and there is a good supply of running water. A thorough wash-out of the milking barn should be done before and after each change of cows. No attempt should be made to wash out droppings *during the milking process because of splashing.*

The milkers must approach their task with clean hands and clothes. The hands *should be washed immediately before each* milking, dipped in a weak disinfecting solution, rinsed, and dried on clean towels. The clothing should be white, laundered clean and tightly fitting. The head should be covered with a cap.

An experienced milker who handles no other part of the cow than the teats, and those as little as possible, and who does not rest his head against the cow's flank during milking, if working under such *favorable conditions as outlined should draw off a high grade of* clean milk which needs only to be kept that way for marketing.

At this stage, however, there comes an opportunity for contamination of an otherwise satisfactory milk—the milk pail. There is probably no more dangerous article in the milking trade than the old-fashioned agate pail which looks clean after a good rinsing but probably harbors millions of organisms in the old milk left in its cracks and crevices or which is waiting to receive all kinds of debris falling into its wide mouth. All such pails should be interdicted!

*The modern pail is made of rustless, non-corrosive, non-absorb*ent material. Its top is almost entirely covered except for a small opening in its center or toward the rim on one side and which can be placed directly beneath the teat. This reduces to a practical minimum the amount of dust, hair, manure, etc., which can fall into it. The pail can be readily sterilized by steam, or better, by hypochlorite disinfection. A solution is made by adding 12 ounces of sodium hypochlorite paste to 1 gallon of water. A tablespoonful of this solution to 1 gallon of water will give a disinfectant wash containing not less than 50 parts per 1,000,000 of available chlorine.

The milk collected from separate pails should always be strained through sterile gauze or non-corrosive fine mesh strainers into collecting vessels. The sediment on the strainers should be burned. A separating centrifuge may be used in place of filters but it must be remembered that it only removes visible dirt.

Whether the milk from separate milkings is to be sterilized at this point, or is to be collected and shipped in bulk for sterilization at a central plant, it must be cooled immediately. It is to be borne in mind that fresh milk is warm and always contains some bacteria. Immediate cooling prevents the further multiplication of organisms in this naturally favorable medium. Cooling to 45° F. (7° C.) or

less may be obtained by placing it in containers immersed in ice water or passing it over cooling coils or cones.

Milk produced and collected in this manner from healthy cows by healthy milkers and maintained at this low temperature until delivered to the consumer should satisfy the standards of Grade A raw milk. If all other conditions of a contract with a Medical Milk Commission have been satisfied it should be certifiable.

There is always a possibility that milk may be contaminated by humans during the milking process and its after-handling. Carriers of virulent streptococci and diphtheria organisms may contaminate milk by droplet infection. Where gross carelessness exists fecal contamination of the fingers may carry dysentery and typhoid organisms and amebic cysts into the milk. For these reasons, commercial milk producers should be liable to examination for the presence of active disease such as tuberculosis, and tests to determine whether they are carriers of any organisms which can gain entrance through milk. They should not be certificated unless they can be rendered non-infective.

The average run of dairies supplying a community does not yet guarantee that the conditions of production and distribution will assure a safe milk supply to the consumers. Except under the most favorable circumstances all bulk milk must be held suspect. This means that it must be sterilized. The method of choice is by pasteurization. This consists in raising the temperature to a certain point for such length of time that the critical temperature of all pathogenic organisms will be exceeded.

The most efficient and widely used pasteurization process is to raise the temperature of the milk to 145° F. (65° C.) and to hold it at that point for not less than thirty minutes. This is known as the *Holding method.* It can only be done effectively in commercial sterilizers, all home contraptions being liable to serious failures and a false sense of security. Most pasteurizers are fitted with thermostatic controls and automatic circulating devices so that all of the milk is kept at the same temperature all of the time. It is essentially a closed process so that no new milk is being added or withdrawn during the sterilization of a single filling. Air heating is also provided to keep the air above the milk at the same temperature as the milk. This prevents the formation of a scum which may protect organisms such as the tubercle bacillus from the full effect of the heat.

Like all automatic devices the pasteurizer must be skillfully operated and tended with the greatest of care. It must be thoroughly cleaned and sterilized between operations.

In contrast to the holding method, milk may be rapidly heated to 158° or 160° F. (71° C.) for fifteen seconds or more and then

mediately chilled. This is the *Flash method* of pasteurization. does not surpass the critical temperature of all pathogens and is erefore *unreliable and is to be employed only on milks of known* cterial content where there is positive assurance that no known *thogenic bacteria exist.* This has been *shown to be practically* possible to guarantee.

Special devices have been developed by which milk can be steurized after it has been put in bottles. It is accomplished by bjecting the bottles of milk to a spray of hot water or a waterth. It is an ideal method if properly carried out.

After the milk has been held at the desired temperature for a cessary length of time it is chilled immediately to 45° F. (7° C.) d is ready for bottling. Secondary contamination can occur at is time by faulty technics in the operation of the sterilizer, espeally by failure to clean the effluent pipes and cocks, and inefficient ttle capping machinery or by human contamination. It is obvious at the bottles and caps must be sterile and the caps tightly fitting. he operation of the feed pipes and rotation of the bottles should be ne as far as possible without the use of human hands. Operators *the entire system must keep themselves scrupulously clean.*

The entire machinery of commercialized production and disibution of milk must be under the supervision of *community* perts and inspectors. Some idea has been given of the many ssibilities for slip-up in the whole process and it is clear that ndiscovered leaks in the chain may result in serious consequences the community, the more so because of the trust placed in the fectiveness of a well organized and protected milk supply.

The small community unit and the individual are not free from e dangers of contaminated milk just because it has been delivered a safe condition. At any time after the original container has been pened and the milk subjected to the air and warmer temperatures rganisms within it can begin to multiply, or it can be re-contaminted. This may occur *without the milk giving any physical evidence at it is unsafe.* There is only one rule which is adequate to insure e *continued safety of open milk. It should be kept at ice-box* mperature and stored only in well cleaned, scalded containers. torage in the original bottles is always best.

The control of the milk supply involves community blanket easures and intra-community general measures. A few specific easures are also employed such as the tuberculin testing of herds nd the Bang and Mastitis tests. For the greater part, however, he whole process after the elimination of these specific possibilities directed against the whole group of milk-borne pathogens. It ses methods that require broad legislative powers and authority o enforce them, the exercise of economic and moral pressure, and

the education of the individual in his own responsibility toward himself and others. The practicing physician can be an important instrument in obtaining the desired end by supporting legislation, the recognition of dangerous carriers, and the instruction of his own clientele in matters of hygienic use of milk and milk products.

PROTECTION BY MEASURES AGAINST SOIL AND WATER CONTAMINATION.

The soil and water contaminants of greatest sanitary importance are human and animal excreta. Infected wastes from factories which utilize animal tissues may make their way back to the soil and the carcasses of animals dying under natural conditions may infect fields and pastures. The sum total of human wastage in the form of garbage and sewage is a potential source of contamination.

Since it is by such processes as these that the life cycles of many living agents of disease are made possible it becomes imperative to operate against them at those points which are at the same time the most practical, economic and effective.

Although there are aspects of the problem which involve inter-community interests it is largely a matter of self defense within the community. The hazard which one community presents to another, or which one social unit holds towards a lesser unit contained within it, results mostly from secondary processes. Thus, contamination of the water supply of one area may result from infected regions in another and infected grazing lands may act as outside sources of contamination of animals and animal products to be used in another community.

The ultimate problem in the prevention of soil and water contamination must rest on the recognition of the earliest stages in the processes of transmission of parasitic agents where they can be effectively intercepted. Ideally this would mean the annihilation of all infecting organisms in the community. Practically, it means the admission that infected hosts exist and the earliest attempt to block their further transmission must take place at the time of, or as soon after their release from the host as possible.

The methods to be applied under the present category will recognize that only two fundamental sources of soil and water contamination exist—(1) Human parasite hosts, (2) animal hosts. All others are secondarily infected sources farther along the line of transmission of disease agents in their passage from host to host.

From Human Sources.—A large proportion of the disease agents found in soil and water are at some time inhabitants of the intestinal canal of man or find egress through it. As a result the earliest attempt to intercept them would be at the time of their discharge. This, in practice, means their destruction immediately

after they have been ejected, or their deposit in such places and under such conditions as will render them impossible of further spread.

In general, human feces is discharged under three conditions, (1) directly onto the soil or into water courses, (2) into independent artificially constructed receptacles, (3) into relatively closed collecting and discharge systems.

The first is the primitive practice of random defecation at any convenient place in fields, woods, streams and any relatively unfrequented locations. Such practices are common among native populations and in civilized communities where artificial conveniences do not exist or there is little time and opportunity to use them. Children are especially prone to relieve themselves wherever they find sufficient seclusion. The ignorant and the insane are notorious offenders.

Even among those who should know better there is a feeling that *it makes no difference in out of the way places. This is especially* likely to occur around camps, along highways, and on the banks of streams.

In the Far East, especially in China, human night-soil has an economic value as a fertilizer and is accumulated in open places until needed. Even where it is not used in this way villagers in native communities establish the custom of defecating in more or less selected spots about the village. This, to a lesser extent, exists in the rural areas of Western countries. All such practices result in a *high concentration of the infective agents in the discharges* at definite locations which are frequently visited by many people. As a result they are pest spots for all who use them. The specific areas are usually chosen because of some existing natural shelter of trees or overhanging bushes or of some man-made structure which gives relative seclusion and protection. These factors keep out the sunlight and prevent rapid desiccation which is to be desired for the destruction of organisms.

The only effectual method for combating contamination of the soil and water in this way is by education of the individual. Even so, this primary conception of sanitation will be violated, and it can only be hoped that anyone who indulges in such a practice out of necessity will have the common decency to relieve himself at some place where there is the least likelihood of others coming into contact with the ground he has contaminated, or where there is no possibility of contamination of surfaces over which rain water can flow and carry his ejected organisms into another's water-supply.

There is no value other than esthetic in covering the discharge with leaves or a thin layer of dirt. In fact, this precaution only adds to the protection from sunlight and drying and is not sufficient to reduce the oxygen to any effectual degree.

Weak antiseptics are ineffectual on loose feces and strong solutions are of use only if they are mixed thoroughly with it and allowed to stand for some time. Chloride of lime thrown over feces may eventually be effective if it is not washed away too quickly by rain.

Human excreta permitted to accumulate in the open is eventually disintegrated by weathering and the action of worms, fly-larvæ, grubs and bacterial activity. Any organisms which are able to persist through these conditions may remain in the soil of the immediate neighborhood for considerable periods depending on whether they can form resisting stages. If so, the water of repeated rains, urine and waste water thrown on the ground can wash them away and disseminate them over wide areas or carry them into wells, springs, ponds, streams and other water sources. The continued promiscuous practice of defecating in the open in and around villages, in the yards of homes, on stream banks and in cultivated fields will eventually result in a heavy concentration of all organisms able to survive. In this way centers of spread are developed for many of the intestinal helminths and protozoa and such pathogenic organisms as the bacteria of dysentery, typhoid fever and cholera.

Community practices such as the use of night soil for fertilization of fields and the construction of squatting places overhanging streams, ditches and lakes are pernicious propagators of organisms like the flukes which live in water and find there their necessary intermediate hosts.

There can be no satisfactory solution to the problem of open defecation other than to forbid it. This may be accomplished by nuisance ordinances and penalties for their violation. The intelligent solution is the installation of sanitary privies along with general education. When night soil possesses economic value it may be collected under sanitary conditions and so treated as to render it harmless without loss of its fertilizing value.

Under certain conditions human urine which contains organisms able to survive in soil or water can act as a source of contamination. This is found most commonly in ditches, army trenches, and mines where the urine accumulates with little opportunity for dilution. Under such conditions where there is some possibility of control, urinals should be provided and penalties inflicted for violation of notices forbidding the practice of open urination. Wherever practical the ground should be drained and chloride of lime spread over all contaminated areas.

The second set of conditions under which human feces is evacuated is represented most typically by the familiar country privy. Here the discharge is collected in independent receptacles and disposed of at the same time; it is neither exposed to the open as in the preceding section nor carried away and disposed of at a distance as in the closed disposal systems to be discussed.

The type of materials out of which it is to be constructed and other specifications will depend to a degree on the temperament and habits of the people it will serve. Natives unaccustomed to the practices of the Occident will not use modern conveniences properly and frequently do so in such a way as to make them more harmful than if they had none at all. In rural districts and small towns without public systems they may be equally misused and ill-kept and can act as potent centers for dissemination of pathogenic organisms.

Without attempting to enter into any detailed discussion of the types and specifications for sanitary privies the following requirements can be set down as common to all simple pit-privies.

1. The pit, trench, or bored hole in the ground should be deep enough so that a considerable quantity of material can accumulate over a relatively long period of time before it is filled. When full it should be completely filled with earth and abandoned for a new site.

2. The platform supporting the superstructure should extend several feet beyond the edges of the pit. It should be of water-impervious material and closed tightly around its edges where it rests upon the ground.

3. The closet seat should be of a type which can be readily cleaned. It should have a lid which automatically closes tightly when not in use.

4. The seat hole should be of sufficient size and such shape as not to permit contact with the external genitalia.

5. The junction of the closet and platform should be tight enough to prevent the entrance of rats, squirrels and cockroaches and the activities of pigs and chickens.

6. There should be a splash-board across the inner surface of the front of the closet which extends vertically from the lower level of the seat to a few inches below the level of the platform.

7. The privy itself should be weather- and vermin-proof and fly-proofed above.

8. The use of a ventilator will depend on the type of privy used. It is ordinarily advised to hasten evaporation.

9. Cement or brick and mortar construction are advisable for the platform and lining of the pit when this is necessary. The superstructure can be of wood. Cylindrical metal risers from platform to seat are used in some instances.

10. The privy should be conveniently located but consideration must be given to the distance from wells, springs and other water sources. The pit or hole should not pass through any porous layer of earth which is suspected of being a water course for a spring or a well. An unlined pit should not extend below the ground-water level.

The simplest indoor privy is the ordinary can type in which the seat is fitted closely to a suitably constructed metal receptacle.

The ejecta is covered with a thin layer of charcoal, dirt, ashes or sawdust after each time the privy is used. It should be emptied into a pit or otherwise safely disposed of daily.

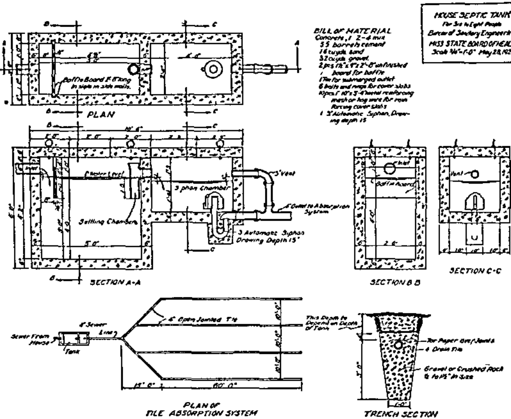
The closet may rest above a large tank built beneath the flooring of the house in which there is a strong caustic chemical into which the excreta falls. The caustic disintegrates and liquifies the feces. The contents of the tank are drawn off at intervals of a few months and hauled away.

When running water is available the privy may be of the water-closet type with a flush valve and a discharge pipe which carries the contents of the toilet into some form of sewage disposal tank or sub-soil filter.

The simplest form of individual disposer is the cesspool. The material from the closet is flushed through pipes into a brick or concrete well-like structure situated beneath the ground at some convenient place at a distance from the house. It is narrow at the top and wide at the bottom. The bottom is left unlined and the top is covered with a tightly fitted lid. The inflow pipe enters the cesspool a little below the ground level. The effluent pipe goes out at the same level but its inner end turns downward so that it is below the water level and empties by siphonage. The effluent pipe passes outward from the cesspool and remaining underground extends on a down grade of 1 inch in 50 feet. Side-branch distributing pipes extend laterally from it. The number and length of the side branches should be sufficient to equal a total length of 40 feet for each person in the household. These pipes are jointed every few feet and the joints left open $\frac{1}{4}$ inch so that the effluvia can seep through into the porous earth. The tank must be emptied through the manhole when the solid materials have accumulated to a point where they will interfere with the siphon.

A septic tank is a concrete or cement tank into which material from the closet is flushed at intervals and allowed to undergo spontaneous liquification. The septic tank is usually rectangular and built in two compartments. The first, or settling chamber receives the inflow near the top at one end and discharges through a pipe directly opposite it which passes through a partition separating the settling chamber from the second, or siphon chamber. A baffle board extends entirely across the upper part of the settling chamber and a few inches away from the mouth of the inlet pipe. The board sticks out about 5 inches above the fluid level and its lower edge is immersed to 10 inches below the water line. The outlet pipe is T-shaped, its cross arm being about 10 inches below the water line and reaching 5 or 6 inches into the air space above the water to act as a vent. The stem of the T is the part which goes into the siphon chamber. An automatic siphon draws the fluid out of the second chamber and discharges it into a series of open-joint pipes

The principle on which a septic tank operates is bacterial decomposition of the organic matter. This results in liquification of about $\frac{1}{3}$ of the solid matter and leaves the remainder relatively harmless as a thick sludge which accumulates on the bottom of the settling chamber. The liquid portion overflows into the siphon chamber from where it is withdrawn by the siphon. This innocuous material is then discharged through the drain pipes and tiles and absorbed by the earth.



Septic tank installation designed and published by the Bureau of Sanitary Engineering, courtesy of the Mississippi State Board of Health

Small community units may combine the sewage pipes from several households into a single collecting system for treatment in a common septic tank but caution must be taken that the tank capacity is not exceeded.

Towns and municipalities with public water supplies are in the position to establish a system of disposal which is entirely closed so far as any individual household or other institution is concerned; that is, the individual unit is not responsible for the ultimate disposal of any of its wastes. This is accomplished by connecting disposal pipes along which the refuse is forced by gravity or

positive water pressure supplied by a pumping system. Surface drainage and rain-water may be collected in the same system as the sewage giving a combined sewerage system (sanitary sewer pipes). Water traps and ventilators in connection with the closets are essential to prevent back-flow and the entrance of noxious gases from the sewers. The prerequisites for the installation of water-closets, and the plumbing in connection with them, as well as the responsibility for their upkeep should be defined in the sanitary code of the community.

There are many methods by which the sewage may be finally disposed of and each community must determine which is the most practical and effective according to the existing natural conditions and economic resources.

The fundamental aim of disposal is to remove harmful and obnoxious excreta from the community in such a way that it is no longer dangerous to health or an affront to the esthetics of the community where it originates or to any other.

Many municipalities are located on or near large bodies of water into which the sewage can be discharged in such a way that the factor of dilution will alone subject the material to natural purification; oxidation will very rapidly make it inoffensive; bacterial activity breaks up and reduces coarse particles; protozoa and fish will consume some of the material; heavy particles will settle out by sedimentation.

The sewer pipes must be carried out into the water in a direction and to a distance to be determined by the direction of water currents and surface winds and the nearness to water-supply intakes, other habitations down stream, the presence of oyster beds in the vicinity, and the lake or river traffic, *i.e.*, the possibility of exposure of those who use the surface in small boats or for swimming and bathing.

It is estimated that other things being equal a body of water will be able to purify about 1 per cent of its volume in sewage.

When natural conditions do not exist by which satisfactory disposal can be obtained by dilution the sewage must be treated by methods similar to those employed in individual or household units but on a large scale. This involves complicated engineering problems in hydro-dynamics of a non-homogeneous liquid suspension which may approximate a fluid volume of many million gallons per day. Furthermore, the discharge of this medium must be interrupted for a sufficient length of time to permit it to be treated chemically or to allow natural physical and chemical changes and biologic activities to operate on it and render it harmless. After these processes have taken place the cleaned fluid must then be moved on to its ultimate point of disposal. All of these together necessitate the construction of some form of receiving basins or

tanks in which the sewage is slowed down or actually stopped for variable periods of time.

The simplest large scale treatment is to have the sewage enter into artificial reservoirs across which the sewage flows from inlet to outlet at a rate of 2 to $2\frac{1}{2}$ feet per minute. This permits the heavier particles to settle out and the relatively clear surface water to flow out through the effluent. There are usually several of these sedimentation or settling tanks in the system so that they can be emptied in rotation and the sediment removed. The sediment, or sludge, is disposed of by incineration or is hauled away and used as filling material in low ground.

The municipal septic tank is a modification of the settling tank and operates on the same principle as the individual or household septic tank previously discussed (see page 519). There are many forms of septic tanks, for description of which the reader must be referred to more exhaustive treatises on this subject. The type in most common use at present is the Imhoff combined settling and digestion tank. In brief, this tank consists of an upper portion into which the fresh sewage is received and the suspended materials settled out. Instead of falling to a solid bottom, the bottom is slotted by overlapping baffles which permit the sediment to slide through slowly into the lower compartment and at the same time prevent the escape of gases through them from below. The sludge which falls through the slots now forms on the floor of the lower compartment or digestion chamber where it undergoes the decomposition and liquefication processes common to all septic tanks. Unliquified sludge must be removed from time to time.

An auxiliary process is resorted to in some plants which increases the decomposition of sludge by substituting aërobic for anaërobic decomposition. This is accomplished by forcing air through the sludge or by keeping the sludge stirred up by mechanical means. This is known as activated sludge. It produces an inoffensive sludge which is harmless and retains its value as a fertilizer.

In all of these disposal systems except that in which simple dilution is effective, either the liquid effluvia or the sludge, or both, must be further dealt with. In many the fluid outflow is clean enough to be emptied into nearby water courses or lakes or distributed into absorbent, porous soils by surface or subsurface drains.

When the effluent still contains much incompletely decomposed materials it demands further treatment. This is carried out most commonly by some form of filtration with or without artificial oxidation. Simple filtration through coarse sand and gravel filters with subsoil open-tile drains is applicable in small plants. They require repeated cleaning of the upper layers of sand.

Broken stone contact beds operate by allowing the sewage to filter slowly through the layer of broken stones and as it does so to

form an organic scum of bacteria and other matters on the surface of the stones. When sufficient sewage has been admitted for one "dose" the inflow is stopped and sedimentation permitted to take place. After one hour the outflow is opened and the tank is emptied from below. This is followed by a rest period of some six or more hours during which time the zoöglea oxidizes under aërobic conditions. A new supply of sewage is then admitted and the cycle repeated. The stone bed must be cleaned at regular intervals when the scum becomes too great and anaërobic decomposition begins to occur.

Oxidation may be improved in contact bed treatment by spraying the sewage over the filter bed instead of letting it flow over it. Because the inflow is no more rapid than the outflow through subsurface drains the tank is at no time full of liquid. As a result oxidation goes on continuously both at the time the sewage is broken up into spray and as it is trickling down through the broken stone. Coke and limestone may be used in place of the ordinary broken stone. In this type also the zoöglea increases after some time to a point where the filter must be rested and cleaned.

The effluent may be further purified by chlorination before it is allowed to enter some natural body of water. It is becoming customary in places to chlorinate the sewage at the inflow into the tank just before it reaches the sprayers.

The sludge which accumulates in all of these systems may be further reduced by oxidation and digestion. The former is accomplished by reducing the water content by further filtration or spreading it on drying beds of sand. Digestion is done in special digestion tanks in which the sludge is kept at a temperature of 78° to 84° F. and anaerobic activity is permitted. Such digested sludge has no further value as a fertilizer.

The concentrated sludge from an activated sludge system is available as fertilizer but all others are usually burned in incinerators, used in public dumps, or towed to sea and dumped.

Other human discharges beside feces and urine can get into the soil and water. They may be the discharges from open surface sores or infected mucous membranes (conjunctiva, urethra, vagina), or they may be materials containing the ova or larvæ of worms which find egress through the skin or mucous membranes. Such materials are more likely to contaminate small areas of ground or bodies of water. Public swimming pools and bathing places are relatively easily polluted in this way and massive contamination by similar means is common in the Ganges River in India.

Contamination can be prevented by rigid adherence to regulations controlling the admission of bathers to public places and sanitary rules to be applied to the owners or operators of the pools and beaches.

In the first place no one should be admitted to a public bathing place who has any visible skin lesions on any part of the body. Physical inspection cannot be expected to be highly satisfactory except under conditions of rigid social control. On the other hand education and the use of warning signs may accomplish much.

All bathers should be required to pass through a soap and water shower before entering the pool. In many modern public institutions the entrance is constructed in such a way that the bathers, in order to get to the pool must pass through a continual shower and walk along a trench containing a foot bath of flowing clean water or water with some added disinfectant. Special straddle showers have been installed in places to insure cleansing of the perineal region.

Bathers should only be permitted to use swimming suits provided by the management. All costumes, towels, mats and such accessories must be sterilized by some accredited method after each time that they are used.

Proprietors and managers of public and private bathing places should be held to rigid adherence to ordinances and regulations designed to meet strict sanitary standards of equipment, cleanliness and purity of the water, sterilization methods, general sanitation of the premises, and adequate approved toilet facilities.

From Animal Sources.—It may be stated dogmatically that all soils and surface waters are contaminated by past or present animal life living on or in it. Most of the ubiquitous pathogenic staphylococci and the potentially harmful colon bacilli are harbored by animals. The anaerobic organisms are almost entirely disseminated in soil by animals, some exception being allowed for lack of explanation of the presence of tetanus spores in virgin soil.

Wild animal life is a continuous source of soil and water contamination but it is seldom intense in any one place except in such areas where herds of animals congregate and in particular spots where secondary parasite hosts exist with a tenacity that keeps up the local infection rate of the larger animal hosts.

Domestic animals are husbanded under conditions which are especially favorable to concentrated soil pollution. This is true not only of the animal pens and yards but also of pastures and meadows where they are allowed to roam.

Animal droppings are the main source of contamination but the types of organisms discharged on the soil in this way are largely limited to those living in or ejected through the intestinal canal. In addition to these there are many organisms which live within the tissues of animals which are returned to the soil when the animal dies and its carcass decomposes on the ground. A lesser degree of contamination results from infected urine and discharges from body

Again the particular organisms concerned must be known and correlated in ways particular to the community. Having established the probable dangers, ways and means can be found for their control. A brief discussion follows of the commonest efforts utilized in enlightened communities.

Because they are instituted and carried out by public authority preventive measures of this category must have: (1) Ordinances, sanitary laws and regulations, and (2) enforcement agencies. The former may originate within the community or be imposed upon it by a larger social unit of which it is a part. Enforcement may similarly be under the control of community agents or those of the greater social unit.

Although many food laws originate out of economic necessity they indirectly meet many of the sanitary needs of the food supply. Each community which is covered by such laws must examine them thoroughly in order to determine just how far they go in insuring protection from factors which are of sanitary concern. For example, a federal law may require that a particular food should contain no adulterants but may be inadequate as a protection against the use of contaminated food.

Local regulations aim to enforce producers outside of the community to raise, prepare and distribute foods in a manner agreeable to the community. This is possible even without control over the outside agents because it utilizes economic pressure by means of competition and the boycott or the confiscation or inadmissibility of undesirable products.

All producers, processors and distributors of food products intended for public consumption can be brought under the control of the health authority by the principle of licensing. The health authority, knowing its standards, can require that they be met before issuing a permit to any business in any branch of the food industry. It must back this up by prohibiting anyone to deal with foods covered by the law who has not received a permit.

Having established its standards, formulated laws to cover them, and given permission to operate under them to individuals and organizations over whom it has jurisdiction, the health authority must establish a machinery to enforce its obligations. Sanitary laws without means to determine whether they are being complied with may be worse than no laws at all because they raise a false sense of security. Once a community has acted to protect itself it has thereby accepted an obligation to the health of its members which it cannot evade.

Control is obtained by the use of sanitary inspectors, medical attachés for special work such as physical examination, quarantine of livestock, biologic tests on food animals, coöperation with other agents which have charge of common interests such as sewage

disposal, water supply, drainage, public buildings and industrial processes, and by the use of police powers and resort to the civil courts when necessary.

It will be most convenient to examine the requirements to be met in certain broad groups of food substances and in some of the principal processes in which food is involved as it passes from producer to consumer.

Meat, Meat Products and Sea-food.—There should be authority to enforce the standard of eliminating all sick animals from herds used as food sources. These animals can only be revealed by frequent inspection by qualified veterinary inspectors. Animals with tuberculosis or positive tuberculin tests, contagious abortion or *undulant fever and positive Bang or Huddleson tests*, anthrax, hog-cholera, generalized actinomycosis, extensive cysticerciasis, foot-and-mouth disease, or having any evidence of visceral or generalized septic processes should be condemned.

All animals to be butchered should be brought on the hoof to a public slaughter house or abattoir. In any well organized community it should be forbidden to slaughter animals privately. The abattoir is essentially a health station at which all animals or their parts which are found to harbor organisms pathogenic for man are rejected and refused entrance into the community. Inasmuch as it deals with dead animal tissues to be used as food it must do so under the highest type of sanitary precautions. A slaughter house should be a model of sanitation and not a blood-smeared shambles. Cleanliness of premises, instruments and personnel are essential and it must be equipped with an adequate, clean, water supply, sanitary toilets and wash facilities. It should be screened and vermin proof and free from rats, mice and the ubiquitous hound looking for food.

All slaughtering should be done under the most approved, humane methods and inspection of the meat and carcasses carried out by veterinarians. Meats, as soon as passed, should be placed in cold storage.

The construction of the abattoir should be such that the materials used are non-absorbing and open to thorough cleansing throughout. Drains should be led off to adequate sanitary disposal systems. The entire plant should be washed down and disinfected after each butchering.

All meats passing the inspectors must bear the tag or indelible stamp of approval of the responsible authority.

Raw meat products in transit can best be maintained in a healthy condition by cold. This can be obtained by freezing or cold-storage. Cold it must be recalled is primarily bacteriostatic and is effectively so to all human pathogens. Refrigeration below 5° F. is fatal to *Trichinella spiralis* after twenty days and to *Tænia*

saginata in six days. All meats should be maintained at a temperature of less than 15° F. from the time of killing until delivery to the consumer. Meats may be kept in cold storage under modern conditions for indefinite periods with perfect safety.

When once removed from the cold, however, they immediately become open to external contamination and unkilled organisms within them can begin to multiply. No meats out of the ice box for more than a few hours are safe for consumption. Household refrigerators should possess an air temperature of not less than 45° F. (7° C.).

Fish must be considered as meat. Those caught and destined for the market must be placed on ice immediately and cleaned at the earliest opportunity. Wholesale collecting platforms should be under sanitary regulations with particular regard to the cleanliness of the water and ice supply and the adequate storage of fish in ice both at the time of their receipt from the individual sources and while awaiting transhipment.

For perfect safety fish should be frozen. They may be kept in good condition for as long as two years if stored at a temperature not over 3.2° F. (−16° C.).

Shell-fish, especially oysters and clams, are frequently bedded at the mouths of rivers and estuaries, the waters of which are almost invariably contaminated. Whereas dilution and artificial treatment of sewage should make these waters free of pathogenic organisms this is not the case in many instances because of lack of sanitary control at the habitations along the river. Because the oyster is a water-drinker and sifts out minute animal life, bacteria and organic matter through its gills, the tissues and juices of a fresh oyster will reflect the bacteriologic state of the water in which it lives. The presence of *E. coli* in measured amounts of shell-liquor is taken as an index of oyster pollution. The counting or scoring is performed as follows:

1. Mix the shell-liquor from 5 oysters.
2. Add 1 cc. of the shell mixture to each of 5 tubes of lactose bouillon.
3. Add 0.1 cc. of the shell mixture to each of 5 tubes of lactose bouillon.
4. Add 0.01 cc. of the shell mixture to each of 5 tubes of lactose bouillon.
5. Incubate all tubes and observe each one for the presence or absence of *E. coli*.

Score 1 for each tube positive in the dilution 1 cc. but not in 0.1 cc. Score 10 for each tube positive in the dilution 0.1 cc. but not in 0.01 cc. Score 100 for each tube positive in 0.01 cc. If the sum of the scores at the three dilutions is greater than 50 the oysters are condemned.

Oysters may be rid of many bacteria by transferring them to clear water in which they will rapidly empty themselves.

No reliance can be placed on this in practice except under the most rigidly controlled conditions. If this proves unsatisfactory chlorination may be resorted to in chlorination tanks where the oysters are kept in water containing 0.5 to 1 part of chlorine per 1,000,000 for twenty-four hours. The water is then renewed and the oysters withdrawn as desired.

Clams, molluscs and snails also take up pathogenic organisms from water and may be the source of widespread infection.

All commercial oyster and clam beds should be licensed and the acceptability of their location should be determined by reference to the degree of contamination of the water and their relation to currents, outlets and water channels. Sanitary control over their collection, storage and shipment must be as rigid as in the case with fish. Clean water and the generous use of clean ice are the only practical and economic necessities for the sea-food trade from the time of the catch to the consumer's table.

Many meat and some sea-foods are processed before delivery to the consumer. Drying, canning, preserving, smoking, salting, pickling, and the addition of chemicals are the most common.

In respect to meat, particularly, it may be stated with emphasis that canning and pickling are the only processes which are reliable. There can no longer be any excuse for the use of chemicals other than the 0.1 per cent limit of benzoic acid allowed by the United States Public Health Service for certain foods. Smoking is too ineffectual in the deeper parts of the meat, especially of pork products, and drying except in well-organized large scale production is open to the same criticism.

Canning is essentially a matter of sterilization and if the raw materials are fit for consumption and the technics employed are above reproach for the particular food concerned the product in the hands of the consumer should be entirely sterile, clean and wholesome. Faults in the chain may result from failure to sterilize the contents of the can throughout and the presence of cracks, holes or leaks in the container.

When canned meats are once opened they are subject to ready contamination and must be kept at refrigeration temperatures. The original can is probably more sterile than other household containers and the food can be kept in it without danger provided it is placed in a satisfactory refrigerator or ice-box.

All commercial establishments which process foods by any of the above methods must be under sanitary control. Samples should be taken from time to time from stock supplies and tested for sterility. The technics employed must meet the standards of the health

authority. The sanitary controlling body must have the power to confiscate undesirable products and force the correction of faults.

The sanitary control of animal herds, abbatoirs, sea-food supplies and the processing of foods protects the individual in the community, and not infrequently the whole community, from a large number of serious and sometimes epidemic diseases. By the proper prevention through these sources of infection, the individual is protected in ways which would in many instances be beyond his own efforts. The householder and the restaurant owner can hardly be expected to be able to apply the methods of detection available to the authorities and the health board must therefore act for him. Except for the control of the water and milk supply there is no greater dividend to be obtained for the community and the individual than through an adequate supervision over meat. It is a food essential to all and consumed by all and it must be clean as well as wholesome.

Vegetable Foods.—Although vegetable and plant foods may be grown in the most highly contaminated soils and waters the infective agents are with few exceptions readily removed by washing. Leafy vegetables and those built up in layers like onions and corms can trap organisms between the layers so that they resist removal by water and can be released only by peeling. Cabbage, lettuce, celery, and other cabbage-like plants are the main offenders in this class and simple washing cannot be relied upon.

Water-cresses, single stalk plants and smooth tubers and fruits are more readily cleaned but may not be completely so.

In general, all raw plant foods are potentially harmful and should never be eaten without thorough cleansing in clean water. In regions where human night soil is commonly used as fertilizer they should not be taken uncooked. Scalding and the use of chemical disinfectants usually so destroy the desirable qualities of the food that nothing is gained by resorting to them.

Public health is generally little concerned with the vegetable foods from the point of view of contamination because so much depends on the habits of their preparation for the table. It is interested, however, in the custom of using human night soil and should prohibit it unless the material has first been rendered innocuous.

Contamination by food handlers in public places is the concern of the health authorities but this aspect of the subject is considered elsewhere as is also the prophylaxis to be exercised by the consumer.

The preservation of vegetable foods by drying, canning, pickling and preserving either sterilizes them completely or acts by bacteriostasis. Improper technics in any of these may leave the contents of containers contaminated and a real source of danger to the consumer. Commercial houses should be held to regulations governing

the processes involved to make sure that they are adequate, and they should be checked up by the examination of random samples taken from stock.

As in the case of meats, preserved vegetables can become contaminated after they have been removed from the can or jar. They therefore should be used immediately or kept on ice. Suspiciously unclean, rusted and bulging cans should be discarded. That even preserved vegetables are not necessarily safe is shown by the repeated instances of outbreaks of botulism due to canned ripe olives which were improperly processed.

Vegetable salads are notoriously dangerous if they are contaminated. Instances of severe enteritis resulting from infected salads are numerous. In some of these the contamination has occurred *after* the salad had been made so that eventualities before and after preparation of vegetable foods must be watched for.

Public Eating Places and Food Handlers.—It will be assumed that the raw food products used by restaurants, lunch counters, soft drink and ice cream stands, sandwich shops, bars and the like, conform to sanitary standards. The health problem involved from there on rests on contamination on the premises.

Food dishes prepared from the stock of milk, meats, groceries, eggs and miscellaneous condiments are open to contamination while being prepared, after they are prepared, while waiting for sale, and during serving. The greatest single source of contamination is from human hands. Although it may be highly unesthetic to have prepared foods and those to be eaten raw, handled directly and thus contaminated with dirt, dead cells, and harmless bacteria it is more than that if those hands harbor pathogenic organisms. These foods will not be sterilized again and the consumer receives a direct dose of potentially dangerous parasites. This is more than imagination when it is recalled that the skin of the hands cannot be made sterile under the best conditions. Food handlers in public eating places are notoriously careless and for this reason every effort must be made by the sanitary authorities to see that the handler himself is not a carrier of organisms which can affect the food. This can be accomplished by certification of all those engaged in the handling and preparation of foods. The certificate should be specific in regard to diseases most likely to be carried by food and on utensils. The responsible organisms are, for the most part, those inhabiting the gastro-intestinal tract but also included are the agents responsible for tuberculosis, syphilis, gonococcal infection, diphtheria, septic sore throat, and those of the common contagious and parasitic diseases. A certificate of clean health signed by a physician licensed in the community and in good standing, or by a physician employed by the health authority, should be necessary before any individual can be employed in connection with the public preparation and

serving of food. The certificate should be renewable annually, after medical examination. The holder should be subject to re-examination at any time deemed necessary by the health authority. It is obvious that the examination must be complete enough to make the certificate more than a mere formality. A test for syphilis and a fecal examination should be compulsory.

In many institutions the cooks and waiters are less sanitary in their habits and clothing than those who do the milking in a common cow barn. Although it is admitted that this is difficult to control by law public opinion should be marshalled against unsanitary establishments of this nature. The proprietor should be made to insist on clean laundered service clothes and cleanliness on the part of the personnel.

A second source of human contamination is the consumer. It is he who is largely responsible for pollution of the utensils. This is harmful to others only when provisions for washing and sterilizing dishes and utensils are inadequate. Krog and Dougherty[1] found bacteria on utensils collected in public eating and drinking places numbered from 10 to 115,000 bacteria per utensil. The wash water in which they were cleaned had bacterial counts from 1600 to 928,000 bacteria per cubic centimeter.

These organisms are apparently cumulative in the wash water and represent the mixed flora of many patrons. It is readily conceivable that damp warm utensils coming from this water and used very soon afterward may convey pathogenic organisms in a viable state from customer to customer. This is more than likely to occur under the conditions met by Krog and Dougherty where it was revealed that in most establishments the glasses and dishes were washed only in lukewarm soapy water after each using and that in beer and alcoholic beverage shops the glasses are washed in hot soapy water only once a day or two or three times a week. Between customers they are mostly washed by a dip in cold water.

A constant flow of hot water or water and steam over dishes and glasses held in racks is completely satisfactory from a sanitary point of view. Water standing in stoppered sinks cannot be retained at a high enough temperature for a sufficient length of time to sterilize more than a single washing of a few utensils at a time. If it is not *too hot for human hands it may not be too hot for resisting organisms.* A satisfactory method in small establishments is to place the dishes and utensils in a wire rack which can be lowered into a kettle of water that is kept boiling. The use of soap is optional so far as bacteria are concerned but is advisable for general cleanliness as it aids the removal of adherent particles and grease.

It is better to air-dry utensils than to wipe them with dirty dish cloths which accumulate filth in the same way as dishwater.

[1] Krog, A. J., and Dougherty, D. S. Am. Jour. Pub. Health, 26, 897, 1936.

Prepared foods (as well as raw foods waiting to be cooked) may be contaminated through the agency of flies and cockroaches. It has been demonstrated many times that these vermin can carry pathogenic organisms on the exterior of their bodies and if allowed to crawl across culture media will leave a trail of multiplying organisms. They can do the same under the conditions found in restaurants where they can gain entrance and deposit bacteria brought in from neighboring privies and garbage heaps. These are again predominantly intestinal organisms such as the typhoid, enteritis and dysentery bacteria.

All enclosed public eating places should be required to be screened by law, and open air counters should have screen or other covers which can be placed over standing foods. Deterrents and poisons should be resorted to to rid establishments of vermin.

Sanitary conditions of the premises in general should be required by law with particular attention to adequate clean toilet facilities, individual hand towels and clean dressing rooms. The cooking compartment should be open to frequent inspection by official representatives of the health authority.

Public Markets.—The users of public markets should be licensed to sell under the provisions of a sanitary code. Most of these provisions are extensions of the requirements made of the producers because there is little difference in the way the materials are handled and stored in each instance. Clean water and clean ice are prerequisites of any public market. All perishable foods should be kept at refrigeration temperatures in show cases or storage vaults and never allowed to warm up. Handling by customers should be reduced to a minimum if permitted at all. Non-perishable goods should be protected from flies, cockroaches, mice, rats, cats, and dogs by suitable barriers.

Those concerned with the oversight of public markets must understand that all foods collected there are older by hours or days than they were at their source and that this means that they can be more readily spoiled. If preservation has been inadequate or delayed, autolysis and bacterial activity has probably already commenced and may or may not have been completely stopped by the processing. But in either case autolyzed meat, fish, eggs and other perishable foods are excellent media for further bacterial activity. The aim of the sanitary requirements is to make sure that a minimim of new contamination results and that new and old organisms are held in check by cold.

The ideal public market should be as sanitary as a restaurant. Because vegetable greens, meat refuse, and discarded produce must be disposed of this can hardly be an excuse for throwing them casually on a saw-dust covered, spit-saturated floor. Receptacles of a sanitary type should be installed at each market stall and their contents duly disposed of to hog raisers, or be incinerated.

The entire market should be rat-proofed and screened if possible. If the latter is not practical all foods should be under cover. (The Public Health Department should see that public markets are not located near dumps and disposal heaps of any kind.)

PROTECTION BY CONTROL OF PRIVATE INTERESTS.

In every permanent community there are private interests which serve the population to an extent approaching public service. They are the barber shops and hairdressing establishments, auditoriums and showhouses, industrial plants and the larger commercial establishments, railway and bus services, and laundries. In these, large numbers of the populace accumulate at one time, or in smaller groups with a rapid turnover; or their clothing is brought together in bulk. In each instance there is an opportunity for the transmission of viable pathogenic organisms from host to host even without their participation in a common act such as the taking of food. In general it is a matter of transmission by contact, either mediate or immediate.

The fact that the services are paid for does not relieve the private interests of responsibility toward the general health of the people they serve. Because they are licensed places of business the health authorities should be able to dictate how they should be run so far as transmissible disease hazards are concerned. This can readily be provided for under a comprehensive sanitary code. The nature of the code will necessarily vary under different social and political systems but there are general clauses which should be common to all.

Barbers and hairdressers come into personal contact with their clientele and it is reasonable to assume that these handlers of other people should be clean. Transmission of disease by them is largely by way of the skin and superficial mucous membranes but their nearness to their patrons also makes them potentially dangerous as disseminators of air-borne infections.

The health authority can act to protect the public by requiring health certificates from these workers with special regard to skin diseases and general diseases with cutaneous and mucous membrane lesions, particularly syphilis.

Because the instruments and linen which they use must be reused frequently sanitary sterilizers should be required for the former and satisfactorily clean and hygienic laundry facilities for the latter.

General cleanliness and personal hygiene on the part of the employees should be required of the proprietor. This may be enforced by the pressure of public opinion and such indirect measures as legal prosecution in cases of sickness known to have been acquired from the establishment and resulting from carelessness on the part of the proprietor. Even for its own good the management should par-

ticipate in the principle of the periodic health examination of employees.

So long as people congregate in ill-ventilated, crowded auditoriums and places of amusement they will subject themselves to opportunities of massive infections by air-borne organisms. In all probability *this cannot be avoided and it is a risk all must run* particularly at those seasons of the year when respiratory infections are prevalent. The only broadly effective effort to prevent such diseases is to remain away from such crowded places and to keep out those who are already infected and in the infective stage. This can be accomplished by regulations in public schools but can hardly be expected in institutions operating for profit. Education alone can bring about public support of any plan to prevent the admission of harmful individuals.

The interiors of many amusement houses never see the light of day and destructive sunlight never has an opportunity to reduce the bacterial content of the air, carpets and upholstery. Deliberate humidification of the air acts still further in favor of viability and spread of microörganisms sneezed, coughed and spat into this highly contaminated environment.

All public congregating places and private institutions of the same nature should be thoroughly ventilated between assemblies. The ventilation system should conform to standards which prohibit objectionable air currents but aim to produce minimal draughts downward toward the floor. Spitting must be absolutely prohibited and punishable by law. The furnishings should be simple and of a type readily cleaned. Seats and chairs in motion picture houses especially are made more sanitary if they have removable, washable, seat and back covers. There should be no carpet on the floor. Non-absorbable floor material is readily washed down and dried between performances.

Adequate sanitary toilet facilities installed and maintained under the health authority are compulsory. The last statement should apply to all lavatories and toilets open to public use. The sanitary *requirements refer to general cleanliness of the rooms and utensils,* the use of sterilizers for combs and brushes, acceptable plumbing and flush toilet and urinal installations, and good ventilation. They should be inspected frequently and there should be penalties for violation of the sanitary code.

Railway trains and cross-country buses to a lesser extent should come under the authority of the political units under which they operate. The new problem of the individual auto-trailer must be solved in this country by the State and municipalities singly or by combined efforts. The chief concern of each of these methods of travel is the collection and disposal of excreta. *If* it is assumed that the toilet facilities are adequate and clean there still remains the

question of disposition. Obviously, no treatise on sanitation can condone the practice of dumping excreta untreated along the highways. There is always the danger of water contamination from such sources. At present, especially in regard to the bus and autotrailer, it appears that the solution will be the provision of individual disposal stations located at convenient points along the main highways. They might consist of miniature disposal plants enclosed in suitable buildings in which there are large deep flush sinks into which pails and chemical treatment tanks could be emptied. If there is a water system available they could be connected with the community supply. In isolated districts the water head could be obtained by storage tanks filled from a surface well pump or an artesian well. The ultimate disposal in the latter circumstances would logically be a septic tank or cesspool.

Cross-country buses equipped with toilets might readily be emptied by suction or siphonage from the tanks at their terminals or other stop-over places. In all instances the immediate collection of excreta should be into tanks or pails containing sterilizing and deodorizing chemicals.

General laundries handle clothing, bed-linen, service linen and toweling, drapes and many miscellaneous materials received from all forms of public and private sources and which have been subjected to all kinds and degrees of infective agents. Sickroom-contaminated linen and dirtied household bed-linen, filthy street and house clothes, dressings from infected sores and soiled hospital gowns, represent but a few of the contaminated and highly infectious materials which are handled by workers in collecting, marking, sorting and treating the laundry.

Although modern methods have largely reduced the possibility of spread of infection from one man's laundry to another's there remains the potential infection of the worker who handles the material.

Sanitary laundry codes must aim to prevent infection of the worker and the spread of infection from the incoming dirty laundry to the outgoing finished product. The general requirements to satisfy these needs are: (1) Collection of individual supplies in separate heavy cloth containers; (2) sterilization of the unopened bags by heat (live steam for fifteen to twenty minutes) before sorting, counting and marking; (3) sorting and packing the finished laundry in rooms or compartments separate from the incoming laundry; (4) physical examination and certification of employees that they are free from any communicable disease.

All ordinary laundry procedures which utilize near-boiling water, steam or steam under pressure, soaps, alkalies and chemicals, either alone or in combinations, effectively destroy all pathogenic organisms.

PROTECTION BY CONTROL OF LIVING ANIMAL HOSTS.

Animal hosts in all classes other than the *Arthropoda* will be considered in this section. (For the control of insect hosts see page 546.)

Rabies is historically among the earliest instances, if not the earliest, in which man recognized the connection between a disease present in a lower animal and appearing in himself apparently as the result of transference. This observation along with other influences, particularly fear, led early to attempts to evade rabid animals and eventually to control them. Today there are many species of animals recognized to be equally as dangerous as rabid dogs and it has become a matter of public interest and mutual protection to control them. This has come about as the result of a long series of brilliant discoveries in the field of epidemiology which together make up one of the most brilliant pages in medical history. For the lists of animal hosts and the organisms which they convey see page 416 (bacteria, viruses, rickettsiæ and spirochetes); page 422 (fungi); page 424 (protozoa); page 426 (helminths).

The lower animals are among the most important factors in human ecology. Man subjects himself to the diseases from which the animals suffer by ingesting their flesh, handling them while alive or their products after death; or subjecting himself to insect disease vectors which they harbor, or infective agents in their excreta and discharges.

In a previous section some consideration was given to the control of animals used as food. Many of these function as agents in the dissemination of disease in ways other than by serving as food and must therefore be subjected to additional control.

At the periphery of the community animals of many types gain admission by deliberate importation, as accidental invaders carried in by man, or by extension of their natural activities. Each community has its own specific problems in this regard. Analysis of animal-borne diseases present in a community gives some indication of their probable outside source, and recognition of the presence of animals outside of the community which are known to be potential carriers is a warning either to prevent their entrance entirely or admit them only after thorough-going inspection. The particular barriers to be set up against them must vary therefore with the diseases which are to be prevented and the avenues of entrance by which the disease agents can be introduced. Much money and effort will be wasted unless this control is scientifically applied.

Quarantine is the common method of control over animals deliberately imported into a community and those which to a great extent come in on ships, trains, carts, etc., as unwanted passengers. It consists in detention of the animals or the vehicles which harbor

them for a sufficient period of time either to permit inspection of the animals or the common carrier, or to permit the disease to appear in animals which at the time may be in the period of incubation.

The diseases for which animals are held in quarantine as a rule diminish in number the larger the community. Thus, there are but few conditions for which animals are refused admission at national boundaries by international agreement while the number at state and municipal lines are many.

Animals are imported for domestic uses of many kinds—food sources, beasts of burden, animal products, to be kept as pets, and as museum and zoölogical specimens (including laboratory experimental animals). They are introduced through natural channels of trade and therefore come in by boat, public and private carriers, or on foot. Because it is impractical to require all animals to be introduced through a single portal, the quarantine and inspection system must be set up at all possible places of entry. Provisions must be made for the detention of animals under sanitary conditions and the inspection must be carried out by veterinarians. Laboratory facilities are necessary to determine the presence of such infections as tuberculosis and contagious abortion (Tuberculin and Huddleson tests.)

No attempt can be made here to name the diseases which should be entirely prohibited because of the great variability in the local circumstances. The economics of the situation might make it absurd for instance to deny the admission of cattle with an infection which already has a high incidence in the community.

In the United States, Federal regulations require certification from the country or district of origin that the imported animals are from an area in which a quarantinable disease has not been present within a prescribed length of time and that the animals have been isolated at the point of shipment for a period varying from fifteen to sixty days before embarkation.

Most quarantine regulations are concerned with diseases communicable to animals as well as to man. The interest in the present discussion is limited to those conditions which are hazardous to man. Below are given the main diseases of animals which can be communicated to man and for which regulation is necessary.

Cattle.—Tuberculosis.—It is very questionable if tuberculin positive cattle should be allowed to enter even though it already exists within the community. Mild, localized infections do not necessarily mean complete economic loss to the owner for the cattle may be slaughtered and certain cuts of uninfected meat passed by the inspector. All cattle with contagious abortion or positive blood tests should be denied admission. Anthrax, foot-and-mouth disease, and rabies are inadmissible. Cattle with septic infections, diseases of the udder and diarrheal conditions should be kept out until the infections have been cleared up.

Horses.—Glanders and anthrax are inadmissible under any conditions.

Hogs.—Trichinosis is the outstanding health problem of imported hogs and yet there is no sure way of diagnosing it during life. Quarantine must be limited therefore to recognizable cases. Heavy importations with *Tænia solium*, cases of foot-and-mouth disease, tuberculosis, contagious abortion, and anthrax should be watched for and denied admission until cleared up, if possible. Swine influenza should probably be quarantined in view of its possible relationship to the human disease.

Sheep.—The presence of anthrax, tularemia, foot-and-mouth disease, and Rift Valley fever are sufficient causes on which to prohibit importation.

Goats.—*Brucella melitensis* infection should be tested for in all goats detained by quarantine. If the test is positive the animal should be rejected. To a lesser extent goats may also bring in anthrax and foot-and-mouth disease, an eventuality which should always be anticipated and prevented.

Dogs.—No dog should be allowed to be imported which has not received preventive inoculation of rabies vaccine. Dogs harboring *Echinococcus granulosus* should either have their infection cleared up or be kept out.

Cats.—To be retained in quarantine until it is established that they do not have rabies.

Monkeys.—Only tuberculosis-free monkeys should be admitted.

Parrots, Parrakeets, Cockatoos and Canaries.—To be quarantined until known to be free of the virus of psittacosis or restricted entirely when known to be imported from established centers of infection.

Specimen animals for museums and zoölogical gardens belong for the most part to animal classes which have representatives among the domestic and semi-domestic animals and are therefore subject in general to the same diseases. Restrictions on their importation should be on the same basis as those of the domestic species. It is even more essential that they be held in isolation at the point of shipment because there is seldom any index of the prevalence of their diseases in the wild state.

The only wild animals of any importance which are capable of carrying human pathogens, and which are introduced into a community by common carriers are rats and mice. They are so ubiquitous and adaptable to almost every climate that it can be assumed that they are present on every ship, and will be found occasionally in freight cars, animal-drawn carts, and more rarely in motor lorries and the larger freight carrying airplanes and dirigibles.

These animals are notorious disseminators of plague and their accidental introduction into communities has been and still is

responsible for epidemics of this disease. As a result, every country which has signed the International Quarantine Agreement, and many others, have adopted general measures designed to prevent the interchange of rats and mice between shore and ship. This is accomplished by allowing a free-space of not less than 4 feet between the wharf and the ship side and placing rat guards on all hawsers, tow and drag lines, and by constant vigilance over all gangways day and night.

If the ship or other carrier has come from a port at which cases of plague or typhus have been reported or cases of either of these two diseases have developed en route no cargo should be removed from the vessel until it has been fumigated and all rats killed.

Under all conditions no litter, fodder, crates, boxes, or manure should be allowed to be removed from any vessel unless it has first been thoroughly inspected and is carried off under strict sanitary restrictions.

All baggage and freight slings, conveyors, ladders, planks, lighters, small craft or any other contrivances which operate between ship and shore or connect the two in any way while in use should be so disposed of when they are idle that no possibility exists for them to act as runways for rats.

Considerable advance has been made to keep down rat infestation in recent years by the construction of rat-proof ships. This is still so uncommon in the shipping at Oriental ports that no reliance should be placed on it in spite of the general cleanly appearance of the vessel.

Airplanes and dirigibles should be subject to similar precautions with allowances for the different conditions under which they are berthed.

Inland quarantine is more difficult to apply because of the great variety and number of small carriers concerned. National boundaries can be zealously guarded because of regulations which require carriers to be halted for purposes other than sanitation. This permits the health authorities to participate in the inspection of the carriers and require the satisfaction of their sanitary codes. They can therefore establish frontier quarantine stations and isolation areas for infected animals and set up provisions for testing for diseases of various kinds.

Rodent control should be an integral part of inland quarantine wherever plague or typhus fever are endemic on either side of the boundary.

The control of infected animals within a community must include measures directed against both domestic and wild animals. Many of the social and political units include areas inhabited by wild animals which perpetuate diseases among themselves and are a constant reservoir of infective agents transmissible to man.

Control measures against infected domestic animals have already been discussed for the greater part under infected food supplies and soil contamination as these are the major processes by which they transmit disease to man. Because they can also produce disease in the human by contact and by acting as hosts to insect vectors of disease agents there are certain measures which should be taken to prevent such diseases at their source. Herd inspection of cattle, swine, horses, sheep and goats should be encouraged by private owners even if these animals are not husbanded for food purposes. Breeders who raise animals for any reasons should be required to weed out all members which show evidence of tuberculosis, anthrax, contagious abortion, glanders, foot-and-mouth disease, heavy infestation with intestinal parasites and tissue parasites such as trichina. Although this may be difficult to enforce by ordinances unless they come within provisions designed to protect the food and water supply or infected animal products for commercial use, the economic importance of a clean herd should be impressed on the owners by every available means.

Non-herd animals such as dogs, cats, birds and other pets and individual members of the herd group which are held by private owners may become a public menace when they are allowed to roam at large or are kept on private premises under unsanitary conditions. Both of these possibilities are controllable by statute. The sanitary code should dictate the conditions under which penned animals can be kept and should prohibit animals which are potentially infectious from wandering free about the community. The only way for example in which rabies can be effectively controlled is by a strict system of licensing of all dogs. Licensing should require protective immunization and all unlicensed dogs should be impounded.

Owners of pet shops should be held liable for the sale of infected animals and their places of business should comply with specific provisions for them in the sanitary code.

The interest of the Health Authority in the wild animals of the community is limited to those types which are known conveyors of diseases communicable to man. In this, every community has its own problems. In one area it may be infected ground squirrels which are responsible for the perpetuation of sylvan plague while in another the reservoir hosts may be the large game animals of Africa which are infected with trypanosomes. The particular animals which are concerned with the propagation of specific disease agents are discussed in a later section of this work. At this time it will suffice to consider briefly the general measures which are applicable in their control.

Rodent Control.—Although the construction of rat-proof buildings entails expense it is the cheapest and most effective method of controlling rats in the long run. The following general specifica-

tions should be followed in rat-proof construction: (1) The ground area should be covered with cement under all markets, abattoirs, restaurants, animal rendering plants, food mills, dairies, animal pens, stalls and stables, all buildings used for the sale or storage of food products, waste bins, manure and offal depositories and toilets. (2) Residences with basements or cellars must have the ground area covered with concrete which is continuous with a surrounding wall of concrete, cement, or bricks and mortar which extends not less than 1 foot above the ground surface. (3) Residences without basements or cellars should be set on pillars not less than 18 inches above ground level. (4) Spaces above the sills between wall boards and joists should be filled with cement or brick and mortar for a height of 18 inches above the sill. (5) All ventilation spaces between double walls, floor and ceiling should be screened. (6) Outside walks and runways should rest firmly on the ground or be edged in. (7) General provisions should be made for cleaning out accumulated wastes beneath buildings erected on pillars and to prevent access of rats to drains, gutters, attics, storage spaces, closets, shelves and out-houses.

Householders and landowners should be required to keep outside premises in a reasonably clean condition. Municipal sewer systems must have their particular specifications in regard to size and accessibility of drains and effective screening where necessary. The general nuisance provisions of the sanitary code will aim to prevent the accumulation of wastes in streets, alleys, vacant lots, etc.

The widespread use of rat traps is an important adjunct to other suppressive measures. The snap trap is the most generally effective but is not desirable where there is danger to poultry, pets and children. The cage trap is useful in the latter instances and where it is desirable to catch the rats alive.

Rat poisons are used where the rat population is large and dispersed as in fields and plantations and in communities where rat-proofing is impractical or too expensive. The most common ingredient is arsenic. White arsenic may be incorporated in any food as a paste or powder but must be in a strength of not less than 10 per cent. A favorite method at present is to cover wheat or other grain with a thin layer of cocoanut oil (1 pint of oil to 100 pounds of grain) and then to powder the grain with white arsenic. Sufficient arsenic adheres to the grain so that 4 to 5 grams of the grain will be fatal to a large rat. It is convenient to put the grain in the center of a square piece of paper about 4 inches on a side and after folding it to twist the ends and make it into a "torpedo." These torpedos are then spread at desired locations about the field or domestic premises.

Thallium sulphate is used in a similar way but the torpedos must contain about 10 grams of the thallium paste-wheat mixture.

Phosphorus and strychnine are no more effective than arsenic and they should not be used because of their danger to man.

Rodents other than rats may be so prevalent in a community as to be an actual source of disease such as plague, tularemia, Rocky Mountain spotted fever and endemic typhus. They are represented by various species of field mice, ground squirrels, chipmunks, susliks, jerboas, tarbagans and gerbilles. Shooting, trapping and poisoning may be necessary to keep them under control or exterminate them if measures fail which are designed to disturb their food supply or interfere with their natural habitat such as thinning-out or burning-over fields and underbrush.

Wild Game Control.—*The limitation of wild game animals to* reservations tends to reduce the contacts between the sources of infection and domestic animals and man. Packs of wolves and foxes may disseminate rabies among domestic dogs so that any effort to keep these wild animals away from human habitations may be an important factor in preventing rabies in isolated communities. Bears, deer, antelope, wild goats, and sheep act as hosts to the rickettsia of Rocky Mountain spotted fever and they should be eliminated from regions frequented by man where this infectious disease exists. *In a similar way the wild animals of tropical Africa* act as reservoirs of the trypanosome of sleeping sickness. Their elimination from regions where the tsetse fly is also present would appear to be advisable if the fly is a common pest in the villages of the district.

Miscellaneous Wild Animal Sources.—These need only be mentioned to indicate the desirability of their extermination or limitation if they are proven in each particular locality to be a source of infection: The bat as a reservoir of rabies virus; badgers and woodchucks and Rocky Mountain spotted fever virus; muskrats and *Pasteurella tularensis;* field mice and the rickettsia of Tsutsugamushi fever; weasels and *Borellia minus;* jackals and hyenas, and rabies; grouse and tularemia; armadillo, bat and opossum, and *Trypanosoma cruzi;* the mink and marten, and *Clonorchis sinensis;* the rabbit and *Pasteurella tularensis* and *Echinococcus granulosus.*

In each instance not only the presence of infection in these animals must be considered but also the opportunity for communication of the disease to man. Otherwise the measures would lead to wanton destruction for no good purposes.

Because many of the causative agents in the animals depend on other vectors such as ticks, fleas, flies and bugs for their transmission to man positive knowledge that the vectors also exist must be determined before any broad destructive measures are undertaken. *This again is a matter of concern only to the community* involved. It must also be borne in mind that a more effectual reduction of the possibility of man becoming infected from these sources

may be obtained in some instances by centering the attention on the extermination of the arthropod hosts.

CONTROL OF INVERTEBRATE HOSTS.

Fish, oysters, shell fish and crabs have been discussed in the section on control of the food supply. Certain species of these invertebrates which are not used as food act as hosts to organisms pathogenic to man. Snails, in particular, are essential hosts for the schistosomes, *Fasciola hepatica*, *Fasciolopsis buski*, and *Heterophyes heterophyes*.

In the regions where these fluke infections are prevalent and fairly well delimited and the actual habitat of the responsible snails is known the molluscan hosts may be greatly reduced in number by the application of unslaked lime along the borders of ditches and canals.

These snails also live only where there are grasses and vegetation so that denuding the banks of infected water courses should help to eliminate them. Sewage and human excreta are excellent food sources for the fluke-bearing snails. For this reason attempts should be made to prevent direct contamination of water by night-soil. Drainage will be ineffectual in preventing propagation of snails which can resist considerable deprivation of water so that this method is impractical. Chemical disinfection of the water is impossible.

PROTECTION BY CONTROL OF ANIMAL BY-PRODUCTS.

Various products of infected animals are capable of carrying disease agents through a number of processes by which they are prepared for trade. Workers who handle the crude products and consumers who use the finished articles may therefore come in contact with these agents and contract disease from them.

The Health Authority of every community is charged with the responsibility of preventing the importation of animal products which may be infective. The greatest dangers in international trade come from animals infected with anthrax or foot-and-mouth disease. Port and frontier authorities are therefore required to set up rigid regulations whereby products imported from areas in which either of these diseases exists are refused admission or subjected to methods of disinfection before entry so as to render them innocuous.

The United States Department of Agriculture[1] lists the following animal by-products subject to regulations for entry into the United States: hides and skins; wool, hair and bristles; glue stock (dried blood or blood albumin, fleshings, hide cuttings, parings, tendons or

[1] U. S. Dept Agri. B. A. I. Order 341 (1934).

other parts of animal products); bone meal; blood meal; meat meal or tankage; bones, horns and hoofs; animal stomachs; glands, ox-gall and like materials; fertilizers; animal manure; cloth and burlap meat covers; hay, straw and chaff. In each particular instance the sanitary regulations designate that the product must be certified as having come from a region free from anthrax, and/or foot-and-mouth disease, and/or rinderpest. In the event that no such certification can be made or is not presented the product must then have been subjected to some process of disinfection before shipment or at the port of entry before it can be passed.

The disinfection processes required are as follows:

Pulled hair, wool, or bristles, by immersion in lime. (Chloride of lime with 30 per cent available chlorine.) Scoured wool or mohair is admissible if it is shown to have reached the stage of preparation for immediate manufacture into yarn, textiles, and other finished products.

Glue stock by treatment with heat 165° F. (73.9° C.); acidulation by mineral acid; or immersion in chloride of lime.

Hides and skins: pickling in a solution of salt containing mineral acid; treatment with lime so as to have become dehaired and ready for immediate manufacture into rawhide products.

Bones, horns and hoofs: by drying and cleaning so that they are free from pieces of hide, flesh and sinews; heat or other disinfectants to be designated by the port authorities.

Glands, ox-gall and like materials: heating at 165° F. (73.9° C.).

Fertilizers: heating at 165° F. (73.9° C.).

Bone meal, blood meal, blood albumin: heating at 165° F. (73.9° C.).

Animal by-products for use as animal food: heating at 165° F. (73.9° C.).

Hay, straw and chaff: by subjecting it in a loosely packed state in tight compartments to the action of live steam, maintaining in all parts of the compartment a temperature of not less than 185° F. (85° C.) for a period of at least ten minutes.

The regulations require in addition that all ships, cars or other vehicles and yards and premises in which restricted articles have been handled shall be cleared of all rubbish and litter, which shall be burned, and then disinfected with either chloride of lime, saponified cresol solution (50 per cent cresol), or liquified carbolic acid at a dilution of at least 6 fluid ounces to 1 gallon of water.

Within the community persons engaged in various activities come in contact with infected animals or their products. Hunters expose themselves to infection with *Pasteurella tularense* by handling the pelts of rabbits, squirrels, and other rodents and by contaminating their hands with the meat, blood and other discharges from these animals. Farmers, dairymen and veterinarians may acquire

undulant fever from contact with live animals suffering from contagious abortion and they may also contract streptococcic infections from infected udders; live-stock handlers may also acquire anthrax, foot-and-mouth disease and Rift Valley fever from sick animals. Sausage makers have been known to contract brucella infection, streptococcus and anaërobic infections and tularemia from handling infected pork meat. There are many instances of anthrax reported as having occurred from the use of infected shaving brushes and furs, and *Clostridium tetani* has been carried by surgical suture material and therapeutic biologic products.

Although the major part of prevention in these instances must rest on personal prophylaxis, general sanitary measures should be instituted against many of them. While regulations governing the operation of slaughter houses and ports of trade will greatly reduce the possibility of infected animal products gaining entrance to the manufacturing processes the owners of the industrial plants should be required by law to adhere to their own sanitary regulations and submit their premises and products to periodic inspection. Certification of the purity of the products might be required in some instances, particularly in the case of biologicals. The industrial owners should be expected to inaugurate a campaign of education among the employees in order that they may be aware of the hazards and participate in prevention. The Workmen's Compensation Act indirectly aids in this way.

Hunters and trappers should be made aware of the dangers of handling wild game known to be potential sources of infection. This might readily be accomplished by distributing informative literature with hunting and trapping licenses.

Farmers, dairymen and all dealers with live stock must be made aware of the dangers inherent in their occupation. Health departments should circularize these workers with instructive pamphlets and this should be augmented by advice from sanitary inspectors and veterinarians.

PROTECTION BY CONTROL OF ARTHROPOD HOSTS.

The defense against disease by control of insect hosts rests on three principles: (1) The use of poisons, deterrents and mechanical barriers; (2) changing the insect's environment or habitat; (3) the control of animals which act as hosts to ectoparasites. Which one or more of these methods will be used against a particular insect is a matter of economic and practical expediency. For example it may be entirely impossible in a given area to drain all breeding places of mosquitoes but it is reasonable to assume that all living quarters will be screened.

With the exception of the rat flea and the yellow fever mosquito,

insect carriers of disease agents are endemic problems, that is, they breed and convey disease within narrow limits and are seldom a matter of concern at the borders of the community.

Control of the rat flea is accomplished in part by rat control (see page 541). Nevertheless, more complete eradication is necessary when any of the flea-borne diseases are prevalent in a community and when these exist in areas from which immigrants are being received on common carriers. The most effective method of control in such instances is fumigation. It is applicable in all spaces which can be made airtight such as the holds of ships, the interiors of railway cars, warehouses, public meeting places and individual *rooms in institutions and households.*

The fumigant of choice is hydrocyanic acid gas. The space to be fumigated must have all openings such as hatches, doors and windows closed and sealed with adhesive paper except for a single opening through which the operator makes his escape. Chests, drawers, cupboards, closets and recesses of all kinds should be *opened and made accessible to the gas. The simplest method by* which the gas may be generated is to place 15 ounces of sulphuric acid in 22.5 ounces of water for every 1000 cu. ft. of space in an earthenware container at a convenient place in the enclosure. When all is ready the operator drops 10 ounces of potassium cyanid into the diluted acid and immediately makes his escape and seals the *exit after him on the outside. A mechanical tripping device to* dump the cyanid may be erected over the acid container which will permit the operator to release the gas while he himself is outside the enclosure. In the above proportions per 1000 cu. ft. of space all fleas (and rodents) will be destroyed in two hours.

Commercial preparations of liquid hydrocyanic acid absorbed *in diatomaceous earth (Zyklon-B)* or wood pulp discs (*HCN Discoids*) are also available and convenient to use. Cylinders of liquid hydrocyanic acid equipped with spraying nozzles are also used.

Under all conditions depending on the use of HCN gas extreme care must be taken to prevent human poisoning. In spaces which can be readily ventilated all apertures should be thrown open wide after fumigation and no one allowed to enter until it has been declared safe by the admission of test animals or until mercuric chloride-methyl orange test papers no longer show a change from orange to deep pink. If natural ventilation is not effective, blow fans should be resorted to to clean out the fumes.

Additional safety to humans may be gained by the addition of a non-toxic gas to the cyanid mixture, which will be repulsive to the extent of becoming unbearable to anyone entering the enclosure until the hydrocyanic acid has has been removed to a harmless amount.

The most highly recommended although not entirely satisfactory expulsive gas is cyanogen chloride. It must be used in the proportion of not less than 30 per cent of the mixture.

Chloropicrin is used but is unsatisfactory because it separates too readily and the tear effect may persist after the room is cleared of HCN. This interferes with after-clearing of the room.

Sulphur dioxide is an effective fumigant but less desirable because of its damage to fabrics and metals. The gas is generated by igniting sulphur sticks or a pile of flowers of sulphur (2 pounds per 1000 cu. ft. of space) in an iron receptacle standing in a water bath. The enclosure must be sealed as in the use of HCN gas. It requires from two to twelve hours to destroy rodents and vermin by this method.

The smoke and vapors from burning pyrethrum powders act as stupefying agents but do not kill insects. After fumigation the inactive insects which have fallen to the floor or remained in clothing may be swept or shaken out and disposed of by burning or the use of insecticides.

Fumigation is effective against fleas, flies, roaches, lice and mosquitoes and is therefore applicable in destroying these vermin under all conditions where they exist in closed spaces.

Mechanical barriers to flying insects are general measures applicable against several species of arthropod vectors.

These free-flying insects arise in their own particular habitats where they may be met by man as he moves among them or they invade his dwelling places in response to environmental stimuli associated with the search for food or favorable combinations of light or darkness and humidity, or for protection from wind and rain. They eventually affect man as they alight on him and obtain a blood meal.

The type of mechanical barrier to be erected will depend on the circumstances under which man and the insect are brought together. Ordinary clothing is effectual in keeping off mosquitoes and sandflies if it is coarse and loosely fitting but the proboscis of the mosquito has no difficulty in penetrating thin, tight fitted articles such as stockings. Under conditions where mosquito- and sand-fly-borne diseases are prevalent, the traveller should protect himself still further by the use of high boots or leggings and under exceptional conditions by gloves and a head net. The latter should hang free from the brim of a wide hat and be tucked in or gathered across the shoulders. It should not come in contact with the skin at any point.

Whenever practical all houses in mosquito- and fly-infested districts should be screened at all times and in most communities at least during the late spring, summer, and early fall months. Adequate screening depends on good building construction. If it is

assumed that all normal openings such as doors, windows and vents are to be screened there should be no unprotected cracks between boardings, wall joints, eaves and basement openings. Should these exist the faults must be corrected by closing them permanently, or if they cannot be closed, they should be screened.

Cloth netting in windows and doors is highly undesirable for several reasons. In the first place it is readily torn and deteriorated by the weather. Secondly, the meshes fill up with lint which interfers with the circulation of air through it.

Rustless wire screening is best. For protection against mosquitoes and flies a mesh of 16 to 18 to the inch is sufficient, but for sandflies and gnats it must be as small as 20 to 24. The screen should be permanently attached to a framework separate from that of the outlet but it should be removable or able to be swung outward for cleaning purposes. It should of course fit the aperture tightly all around and be weather stripped if necessary. Screen doors should open outward. When practical, double screen doors with a vestibule between them are advisable.

All sleeping porches and galleries should be screened if they are to be used for any purpose after nightfall. Because many of the mosquitoes are night fliers all windows and doors should be closed in the late afternoon before the insects have begun to fly.

Collapsible screen rooms, which can be transported and erected at suitable spots in construction camps, field laboratories, etc., are convenient protections to workers who must sleep in the open.

A modern sophistication is to charge metal screens with low voltage electric currents in order to destroy as well as bar, all flying insects that come in contact with them.

When for any reason, screening of houses and rooms is impractical, as it is in most native huts in the tropics, it is necessary to resort to the use of mosquito bars or nets over the beds. These are generally made of cotton netting suspended from extensions of the bed posts to a height of several feet, or hung from any convenient structure above the bed. The netting must hang completely around the bed and preferably be tucked under the mattress. Where there is no danger from vermin on the floor, the lower edges of the net may be weighted with rope or small chain and allowed to rest on the floor. Entrance is gained into such a net by raising the edge over the head or through a slit-door-like effect on one side made by cutting the net and having the cut sides overlap for at least 3 feet. In the use of all nets and bars the user must make sure after he is inside that he has left no openings. Mosquito bars must be kept in good repair for it is not uncommon to find tears in the corners where tapes have been sewed on for tying up the net.

In institutions such as hospitals and in some private homes it is possible to erect permanent wire screen-rooms over the beds. It should be routine to drop all mosquito bars before dark.

Portable bars should be used by all travellers in malarial and yellow fever districts who go cross-country where no rest house facilities exist.

The screening of railway coaches and other vehicles in which passengers travel at night is as essential as with any sleeping quarters.

In the daytime, all screened rooms, porches and conveyances must be thoroughly aired and a search made for mosquitoes which might have gained entrance to them, and the mosquitoes destroyed.

Electric fans and punkahs mechanically blow mosquitoes away and are useful for those who wish to sit around out of doors in the evening. Additional protection may be gained by the use of canvas stockings or boots drawn up over the trouser legs or high up beneath the skirt. Or the legs and feet may be placed in a sac which pulls over the trousers or skirt to well above the knees and is held in place across the lap by a draw-string.

The insecticides and methods by which the environment is made unfavorable to insects vary widely with the insects concerned. Because they must be dealt with individually and are in general inapplicable against wide groups of insects, they will be considered under each particular type of insect host.

Mosquitoes.—Reference to the habitats of the various types of mosquitoes reveals that the methods of control against one type may be ineffectual against another.

Anopheles is a natural water breeder, favoring streams, bayous, ponds, lakes and ditches in which water plants are growing. They also develop in the hollows of tree stumps and the recesses of canes, palms and fiber plants. Seldom travels more than 100 yards away from its breeding place.

Aëdes is a domestic mosquito which prefers to breed in still water. It selects standing, clean water in tubs, tin cans, buckets, bottles, shells, tree-holes, clear water drains and quiet rock-pools. One species, *A. sollicats* breeds in salt marshes. May travel a few miles.

Culex is a dirty water breeder and deposits its eggs in gutters, drains, ditches, sewage outflows, dirty receptacles and stagnant pools. Found mostly around human habitations but may also breed at far distances from them.

Anopheles mosquito control is primarily one of draining natural waters when this is practicable, or treatment of the water to make it unfavorable for the growth of the larvæ. The first should be directed against all unnecessary accumulations of water within the community and in a radius of a few miles surrounding it. These should be completely drained and filled whenever possible. If for any reason it is not practical to go to this extent the natural outlet should be made more effective by deepening or straightening the channel. When this is done the drain must be kept free of vegetation along

its borders and no standing pools must be permitted to remain at low water. All borrow pits must be filled in after construction work of any kind. Subsoil drainage eliminates the possibility of creating new breeding places and is the method of choice.

Trees around habitations may be made inaccessible for breeding by efficient pruning so that there will be no accumulation of water anywhere in them. The same applies to the thinning of vegetation around houses.

Aëdes mosquito control is largely a matter of preventing this mosquito from breeding in domestic containers. The proper disposal of tin cans and bottles, and care of waste heaps to prevent accumulations of water in them, and attention to gutters, drains, cisterns, wells, pools and tree-holes will aid greatly in reducing the prevalence of this mosquito locally. It must be remembered that *aëdes* may develop in flower pots and other water containers *inside* of screened houses if a female *aëdes* happens to gain admission to the house or its eggs are carried in in water.

Culex mosquito control is accomplished by eliminating breeding places which are made in great part by man for drainage and sewage purposes. All outflows from kitchens, washhouses, pumps, septic tanks and cesspools should be through subsoil drains. When this is impossible the drains and ditches should be smooth and free from standing water at any time, and kept cleared of vegetation. The grade should be such as to insure a rapid flow.

The use of an oil film on water which prevents surface living larvæ (*anopheles*) from using their siphons and also acts as a poison, is to be looked upon as a method of control supplemental to filling and draining or to be used when these larger methods are impractical.

The oil of choice should be light and dispersable over the surface of the water. Crude oil distillates meet these requirements as do coal oil alone or crude oil and kerosene in the proportion of 3 to 1. It may be sprayed over the water from a knapsack spray or a compression spray carried in a boat. The oil must reach the edges of the body of water where the mosquitoes breed and must be used in sufficient amount to make a continuous film on the water. If the water surface is subject to winds oiling must be frequent in order to keep the film intact.

The old drip-barrel method is least economic under most circumstances and is only applicable over narrow streams with a not too rapid flow. It is difficult to regulate the rate of drip required to feed the oil on the water in such a way as to keep up a constant film under changing conditions in the stream.

Paris green is the most effective larvicide and is adaptable for use on bodies of water too large for the use of the oil film or too thick with vegetation for oil to be effectively applied.

Paris green is insoluble and does not affect the potability of the water. It is used in the amount of 10 grams of Paris green to each 90 square meters of water surface to be treated. The amount is then diluted with 100 times its bulk of fine, sifted dust. The mixture is sprayed by hand, throwing it into the air on the windward side of the body of water. The insoluble film settles and spreads by surface tension over the water surface and acts as a poison to larvæ feeding at the top. It is ineffectual against culex larvæ because they are under-surface feeders.

Culex larvæ in stagnant drains and impounded puddles of dirty water can be killed by dropping a lump of carbide into the water. It is far less trouble to clear up the pools once and for all than to have to resort repeatedly to chemical methods such as this.

Surface feeding minnows (*Gambusia* spp. and others listed on page 432) are natural enemies of mosquitoes because they feed on larvæ. They should be encouraged to grow in bodies of water where they may be found, but can be planted in artificial waters such as reservoirs, ornamental lakes and ponds, fountains and even small water containers such as cisterns, water-plant aquariums and the like. Top minnows indigenous to the locality generally thrive better than imported types. It is important to make the margins of the bodies of the water accessible to the fish by clearing out all unnecessary vegetation and floating débris.

Because *Aedes* breeds mostly in water in small containers the fish to be used to control this type of mosquito must be adaptable to a confined existence. The chalaco (*Dormitator latifrons*) and the life (*Pygidium piuræ* of Peru) have been found to be effective in this way in yellow fever control (Connor).

Mosquito control in general involves broad community programs and individual efforts. It must always be carried on, on any extensive scale, in the most economic and at the same time, most effectual way. Large sums of money must be expended in any satisfactory program which depends on filling and draining, not only because of the initial expense of labor and material, but because allowance must be made for property rights and the project must be maintained. No drains and ditches will remain larva-free over a length of time unless they are carefully tended. Vegetation must be kept down, pools and eddies prevented, and the margins kept clear. It is often necessary to vary the level of the water from time to time in lakes and reservoirs in order to disturb eggs and larvæ from their adaptation to the changed conditions along the shore-line.

Individual efforts need involve little expense and may be no more than good housekeeping on the premises. The cumulative effect of many individual efforts will frequently be more effective than misdirected efforts of overenthusiastic public health idealists.

Individuals can protect themselves from the bites of mosquitoes to a limited degree by anointing exposed parts with some odorous material dissolved in oil which is repellent to mosquitoes. Those substances most commonly employed are citronella, pennyroyal, eucalyptol, camphor, peppermint, menthol, cinnamon oil and creosote. The oil base is frequently cocoanut oil or some other bland, non-irritating vegetable oil which will not become rancid. The method is of value only for short periods as its effect soon wears off as the oil disappears and the volatile substances evaporate. It is never completely reliable at best.

In the tropics it is not uncommon to burn some form of incense powder in which pyrethrum has been incorporated as a general repellent. Its use is directed against mosquitoes which tend to accumulate beneath tables, chairs, etc., in closed rooms. Like other repellents, this method is only partially effective and should not be relied upon further than as a nuisance control.

Fleas.—The control of the rat flea rests largely on the control of the rat (see Rodent control, page 541).

Man's direct contact with fleas results from infestation of his living quarters with fleas brought in on rats or animal pets or by handling animal hosts when hunting and skinning game, examining rats, tarbagans, jerboas, squirrels and other rodents for infected fleas or signs of epizoötic plague, and from frequenting grounds and property on which these animals have their nests or burrows.

The flea does not remain permanently on its host nor are its eggs attached to the hairs among which they are laid. Instead, both the adults and eggs drop off to the ground or floor. Breeding and metamorphosis take place in cracks and crevices of floors in the nests and burrows of their host animals. The eradication of these pest spots therefore constitutes one of the best efforts to eliminate future generations of fleas. Particularly, this should be done around homes and their outhouses. Kerosene poured into such nests will destroy all developmental stages. Fleas in the dirt of animal runs, dog kennels, and bare compounds may be kept down by spraying with heavy brine. Strong sunlight and dry ground are inimical to the growth of pupæ and larvæ. Within the house, powdered napthalene spread lightly over the floor in a closed room and allowed to remain over night will kill the fleas in the carpets and crevices of the floor. Solutions of formaldehyde, carbolic acid, and bichloride of mercury, and infusions of tobacco are effective pulicides against the adult flea.

Those who handle infested hosts should use extreme personal precautions in regions where flea-borne diseases are endemic or epidemic. The hands and neck should be covered during times of epidemic when examining rats for plague fleas.

Ether and chloroform sprayed on the animals before they are

removed from containers will stupefy the fleas which can later be combed out and handled without danger. Only an excess of these anesthetics will actually kill the flea.

Patients with plague and typhus should be completely protected from fleas by enclosing them within a fine mesh netting with a mesh not larger than 20 to 24 to the inch.

Aromatic oils applied to the body are flea repellents but are unreliable for safe prophylaxis against flea-borne diseases.

Lice.—The human body and head lice pass their entire life cycle on the body and clothing of man; the former largely in his clothing and the latter on the hair. For this reason defensive methods against them must involve not only the removal of the parasites from infected individuals who can pass them on to other hosts but the sterilization of the clothing on which they can be carried.

The body louse is readily removed by a hot bath with soap and water, but the head louse being among the long hairs of the body and its eggs attached to them requires more heroic methods. The nits may be killed along with the adults by soaking the hair with a mixture of equal parts of kerosene and olive oil and allowing it to remain for twenty-four hours. At the end of that time the hair is washed with weak vinegar, which loosens the nits, and enables them to be removed with a fine comb. When the hair is excessively matted it might be necessary to cut much of it off.

Clothing is most effectively deloused by heat.

Individual clothing is readily deloused by boiling for even a few minutes or if this is harmful to the clothes by immersion in water at 158° F. (70° C.) for thirty minutes. Hot ironing along the seams will often be sufficient to kill the young forms in lightly infested clothing but this method is not applicable on a large scale.

Widespread dissemination of lice under domestic conditions is largely prevented by the general laundry. The ordinary processes of the steam laundry will kill all stages of clothes lice.

In the army, work camps, expeditions, etc., wholesale delousing is done with portable steam sterilizers or various improvised forms of apparatus which use steam, hot water, chemicals or fumigants. The Serbian barrel is a steam process by which a fire is built under a metal boiler with a perforated bottom and a lid. The clothing is placed in the barrel and subjected to the steam rising through it from the barrel for a period of one hour. Leather and rubber are destroyed by this process and should not be used in it. Hot-water sterilization is carried out by immersion in hot water in large metal water heaters.

Chemical delousing is most effectively done with kerosene but it is too expensive on a large scale.

Fumigation is effective in killing all stages of lice except the nits.

It must be followed therefore by one of the other processes in order to insure complete delousing.

The common fumigants are hydrocyanic acid gas, carbon bisulphide and chloropicrin. The first is dangerous to human life and must be used with caution in tightly enclosed chambers. It is used in this way to remove lice from clothing in storage. The gas must be able to penetrate all parts of the clothing. This is accomplished by spreading it out on racks or hanging it on hooks or by forcing the gas into the chamber by vacuum. Precautions must be taken against poisoning after opening the chamber by allowing long and effective airing.

Carbon bisulphide is explosive and is to be used with caution. It is used by placing 1 pound of the chemical for each 100 cubic feet of the space in a container high up near the top of the enclosure. As it evaporates the heavy gas percolates downward among the clothing. Exposure to the gas is continued for ten to twelve hours.

Chloropicrin is introduced into the delousing chambers in the amounts of 4 cc. per cubic feet of space and allowed to act for thirty minutes.

Personal prophylaxis is an essential part of louse control. Frequent bathing and cleanliness of body and clothing will prevent all but temporary accidental infestation. When conditions make this degree of precaution difficult to attain routine sterilization of clothing must be resorted to.

Flies.—The common house-fly is a manure and offal breeder.

Control of these vectors of pathogenic organisms is primarily one of community sanitation in general. The open sewer affords innumerable opportunities for the house-fly to undergo its complete life cycle without disturbance. The adult female deposits the eggs in the exposed excreta or garbage. In about a week the maggots leave this material and enter the ground where they pass through the pupa stage and emerge as adult flies in a few days. Any unsanitary conditions of waste and excreta disposal therefore act as breeding places. Manure piles, unprotected privies, domestic animal pens, garbage cans and garbage heaps, open drains, stagnant street gutters with street sweepings accumulated in them, open, unprotected markets and meat stalls, and the waste heaps from kitchens and industrial houses which use animal tissues are the common sources to which to turn in a search for the place of origin of fly pests.

The control of these factors has already been discussed under general community sanitation measures. In addition, individual efforts may eliminate many breeding spots. All garbage cans should have fly-proof covers and no offal or rubbish should be permitted to remain in the open, at least for more than a few days at a time. Manure heaps should be enclosed as far as practical within screened

enclosures or in bins. If this cannot be done the pile may be burnt over by scattering papers on top of it, igniting them, and thus destroying any eggs which are already present and making the surface of the manure-pile unattractive for further oviposition.

Chemical treatment is likely to be too expensive for continued use. The most effective material is hellebore. One-half pound of powdered hellebore to 10 gallons of water for each 8 bushels of manure is poured over the surface of the manure pile. (Boyd).

As it is practically impossible to eliminate house-flies completely it is necessary to obstruct their entrance into buildings by the use of screens. This is essential wherever food products are being handled and includes markets, groceries, meat stalls, restaurants and private households. Food materials exposed for sale must always remain under some fly-proof cover of glass or wire-screening. The sanitary code should include this necessary provision.

Even with effective screening some flies usually gain entrance indoors through doors and windows as they are opened and shut. These can be eliminated readily by fly swatters, poison and fly paper.

Flies are a particular menace in private households where there is sickness due to organisms of the intestinal groups, typhoid, dysentery, enteritis. Meticulous attention under these conditions must be given to disposal of excreta and left-over foods, and the cleanliness of bed linens and bed-clothes. A constant vigilance is required to kill immediately all flies which get into the sick-room.

The home kitchen under all conditions should be protected from flies, and food stuffs, milk bottles and soiled utensils should not be permitted to stand around to be contaminated by disease-spreading flies.

Many of the myiasis-producing flies are carrion breeders and their elimination depends on the quick removal of all animal carcasses and animal wastes. Dead dogs, cats, rats and larger animals should be quickly disposed of by burial or incineration. They should not be carried away and dumped elsewhere as this only transfers the nuisance to another neighborhood. Those flies which breed on the hairs of living animals can be kept down by cleanliness of the animals. Cows, sheep and horses ought not to be neglected entirely but should be subject to frequent bathing or cleaning of some sort.

The defense against the tsetse fly rests largely on protection from its bite by adequate screening and the use of head nets in heavily infected districts. The fly is on the wing mostly at mid-day so precautions are especially necessary at this time, a fact to be noted particularly by those whose work carries them into the bush.

Some degree of control over the tsetse fly may be gained by noting their breeding places which are not often more than 100 yards from where the fly is encountered, and then clearing out the underbrush

at that place. Few flies will cross a bare clearing around a village over 100 yards or more in width unless they are carried over by man or animals. Flooding of breeding grounds will prevent the female from depositing her eggs at the most favorable spots at the bases of small shrubs and trees. *Glossina palpalis* which breeds near water margins may be considerably reduced by combining denudation of the margins of streams and rivers for a distance inland of some 50 yards with clearing out of the banks and straightening of the water courses.

Bed-bugs.—These insects are domestic breeders and can only adequately be attacked by household cleanliness. Repeated washing of furniture with soap and water, giving particular attention to cracks and crevices, will prevent the deposit of eggs in these places and remove eggs and immature forms. The floor should be washed frequently with soap and water and treated after each washing with an oil drench. Kerosene, turpentine and scalding water poured into floor cracks will kill eggs and nymphs. In heavily infested rooms it may be necessary to remove loose floor boards and wainscoating in order to get the oil to the nests. All stages of bed-bugs can be killed by cyanide gas used in concentrations four or five times that used for rats (see pages 141, 541, 547).

Bed-bugs also must be eliminated from the seams of mattresses, sheets and blankets, and from rugs and carpets. Complete sterilization of these is best accomplished by steam or hot water or by fumigation.

Pyrethrum insect powders will stupefy immature and adult forms. The inactive insects must then be killed by one of the other methods.

Ticks.—A knowledge of the life history of the tick reveals a number of possible places at which defensive measures might be taken against it but some of which would be highly impractical. Little can be accomplished for example against the nymph stages in the ground, and in many instances it is impossible to attack the engorged females and seed ticks which are widely dispersed among the grasses and natural shelters on the ground unless the whole area can be effectively burned over.

Some eradication is possible by the extermination of the small animal hosts of the seed ticks—ground squirrel, chipmunk, woodchuck, weasel, pine squirrel, field mouse and wood rat.

The most practical method is tick eradication on the large domestic animals. These animals pick up the adult tick from the pasture lands and forests and carry them into non-infested lands and herds. If these ticks are not destroyed immediately they will drop off and start a new cycle of generations in the previously clean area. For this reason, tick eradication is frequently an important community problem. Sanitary regulations are often invoked to prevent the transportation of cattle, and sometimes other domestic animals,

between communities, unless adequate eradication measures have been used and the animals have subsequently been passed by inspectors as tick-free.

Tick eradication on the large scale must start with the wild animals which should be kept away from all localities where domestic animals graze. Many of the smaller ones can be trapped or shot but the deer, bears, etc., cannot, in most instances, be so wantonly destroyed. If they cannot be frightened off, the domestic animals must be held in bounds by fences or herders.

The domestic animals should be examined frequently for ticks, especially between the months of late winter and mid-summer. When found the ticks may be picked off by hand, collected and burned, or when many animals are to be handled, they may be dipped. A standard arsenical dip consists of sodium carbonate, 24 pounds, trioxide of arsenic, 8 pounds, pine tar, 2 gallons and water to 500 gallons.

Individual prophylaxis in infected regions is practiced by removing all ticks quickly by the use of ammonia, turpentine or kerosene and immediate cauterization of the bite with carbolic acid. Herders, farmers, field workers and hunters should examine their bodies frequently for ticks. Leggings and high boots are a protection but only if the tongue flap and eyeholes are sealed off from the interior of the boot.

The domestic tick which lives in beds and floor cracks in native huts in the tropics is killed by removing all articles from the hut and subjecting them to strong disinfecting solutions or scalding water. The interior of the hut should be cleaned in the usual way. All old mattings and unnecessary furnishings should be burned.

Mites.—The common itch mite, *Sarcoptes scabiei*, is transmitted directly from man to man by contact or through common clothing and bed-linen. Prevention of this transmission is a matter of eradication of the organisms from the human host by the use of sulphur ointment, the avoidance of contacts with infested humans and by sterilization of clothing and bed-linen by boiling.

The various species of "red-bug" are so ubiquitous as to be almost unavoidable. The use of repellent oils and ointments is only mildly effective. Water-tight leggings and boots will keep them off the lower extremities but if a person sits on infested ground or walks among grasses and berry bushes containing these mites they can readily penetrate open-weave clothing and get in through the waist band, collar and buttoned flaps.

Infestation with grain itch mite (*Pediculoides ventricosis*) and kedani mite (*Trombicula akamushi*), the mite found in tobacco (*T. schuffneri*) and palm-oil (*T. deliensis*) plantations, and the coolie-itch mite (*Rhizoglyphus parasiticus*) are occupational diseases difficult to avoid. Rubbing the hands and arms with oil of

eucalyptus is said to act as a deterrent. Sterilization of straw by steam before it is used by mattress makers may help to prevent grain itch. Growing vegetation may be cleared of mites by spraying with a mixture of flowers of sulphur in kerosene, creosin or soap wash.

It is obvious that mites should be removed as soon as discovered on the skin and their bites touched with a germicide to prevent secondary infection.

PROTECTION BY RESTRICTIONS ON HUMAN HOSTS.

The interests of the community require the restriction of the activities of individuals who carry certain infectious agents insofar as they may be disseminators of these agents in the community. This involves curtailment of individual rights and requires the force of law behind all efforts toward restriction. Moral obligations may enhance the ease with which restrictive measures can be enforced, and education will in general be a necessary accompaniment, but these two supplemental forces cannot alone be sufficiently binding to be trustworthy.

Health laws must be reasonable, logical and based on scientific knowledge. Too often they are founded on misinformation and prejudice and in many cases permit dictation and interference by special privileges. The extent to which they can be applied is necessarily dependent on the general enlightenment of the community. For these reasons, education should precede, or at least be contemporary with legislation. The show of force can only exceed by little the willingness of the community to accept self-imposed restrictions, and so long as this warning is ignored the laws will be more frequently broken than complied with.

The particular disease agents which it is desirable to check by restriction of carriers are determined by knowledge of the agents which might be imported into a community and those which are already there and whose spread must be prevented.

National boundaries and ports of immigration must be guarded by national health agencies acting under national laws. These agencies recognize certain diseases which must be kept out of the country completely or which must be brought to a non-infective stage or cured before the individuals suffering from them may be admitted. They have gone still further in certain specific instances by requiring that all individuals who desire admission must first be made immune.

National quarantine in the United States is limited under ordinary conditions to detention of patients and exposed contacts with smallpox, cholera, yellow fever, plague and typhus fever. Patients with trachoma and leprosy are not admissible.

There are three health agencies concerned in protecting international health. (1) The International Office of Public Hygiene in Paris. (2) Foreign Health Inspection Service. (3) The National Public Health Service of the country concerned.

The International Office of Public Health is a central exchange agency which receives communications from the Health Section of the League of Nations, the Pan-American Sanitary Bureau, the Sanitary and Maritime Council of Alexandria, and other agencies, on the prevalence of internationally quarantinable diseases present in the regions under their jurisdiction. By this means all governments which participate in this world-wide organization can be cognizant of the health conditions in other countries from which they might anticipate the receipt of immigrants.

The Foreign Inspection Service is an extension of the health authorities of one country into the consulates and metropolitan areas of other countries. Information from these centers supplements the reports received from the larger International Health Agencies and the government officials connected with them participate in the inspection and certification of individuals and common carriers leaving for the country which they represent.

The National Health Service is the sanitary branch of a government located at the ports of immigration and which is directly responsible for the admission, detention, or deportation of individuals arriving from foreign countries.

A community having determined what disease conditions it desires to prevent by peripheral barriers, and being cognizant of the probabilities that individuals with these diseases or who have recently been in contact with them, will be brought to it from particular areas, sets up a quarantine service to administer its regulations. The regulations aim toward three ends: (1) the *isolation* of individuals presenting themselves with diseases which are communicable and inadmissible or are carriers of organisms of these diseases; (2) the *quarantine* or detention of those who have been exposed to a communicable disease for a period of time equal to, or longer than, the incubation period of the disease to which they have been exposed; (3) the unimpeded admission of all eligible immigrants who have a clean bill of health insofar as communicable and inadmissible diseases are concerned and have not been exposed to such diseases within the period of incubation or have received preventive immunization against certain diseases within a prescribed period of time. The "unimpeded admission" of the latter group should be the ultimate aim of national quarantine. If the provisions governing quarantine and isolation are carried out effectively at the port of embarkation, there should be a minimal delay, if any, in the admission of most immigrants. Furthermore, communicable diseases of the type concerned in international

quarantine, are for the most part communicable only under certain circumstances and by the aid of additional agents. Thus, typhus requires fleas, cholera vibrios must gain entrance to food and water, yellow fever needs *aëdes* mosquitoes.

If sanitary conditions on ship board and at the port are such as to preclude the activity of these necessary adjuncts to the spread of disease, the sick patient need only be treated as a sick patient and all others can be allowed to pass with precautions. This ideal state is nearing an accomplished fact in the larger, most thoroughly organized ports of the western world. The health authorities at these points are so familiar with the great majority of carriers coming to them that they are acquainted with the sanitary condition of each one of them and know that the passengers and crew have been adequately scrutinized and certified as having a clean bill of health. By means of radio communication they can also be informed of illness on board the carrier before it arrives at the port and so are able to deal with it safely and expeditiously when it comes in.

Until recently the speed of transoceanic travel has been slow enough to occupy more time than the usual incubation period of most of the communicable diseases so that if no new cases have broken out on the voyage the ship journey itself has acted as a period of quarantine. On short trips this has never been so and in recent years the time of travel has been so cut down as to make it ineffectual in many instances. The airplane and dirigible have added to the hazard by being able to leave one country in which quarantinable diseases are endemic, jump completely over intervening countries to their destination which may long have enjoyed immunity from these diseases because of natural barriers. The possibility of the dissemination of yellow fever from western Africa to India, the Orient, and the Near East is a case in point.

National authorities reserve the right to tighten up on their restrictions at any time. When a communicable and quarantinable disease exists in undue or epidemic proportions in an area from which immigrants are expected, it may be necessary to deny admission to anyone from this area for the duration of the emergency. Also if a country itself is having an epidemic of a disease such as smallpox, for which there is an active immunizing agent, it may require that all coming into it be made immune.

Inland and district quarantine rest on the same principles as international quarantine but are generally more flexible. The state, province, and municipality, like the country, must know its own communicable disease hazards. Experience may reveal the presence of certain infective agents in a community but does not give accurate information on prevalence. In order to obtain current information on the morbidity rates of these diseases the health

authorities usually require the practitioners of medicine to notify them of all cases coming under their observation.

The model morbidity law of the United States Public Health Service lists the following notifiable communicable diseases:

Actinomycosis	Ophthalmia neonatorum
Ancylostomiasis	Paragonimiasis
Anthrax	Paratyphoid fever
Chickenpox	Plague
Cholera, Asiatic	Pneumonia (acute)
Dengue	Poliomyelitis (acute infectious)
Dysentery	Rabies
(a) Amebic	Rocky Mountain Spotted Fever
(b) Bacillary	Scarlet fever
Favus	Septic sore throat
German measles	Smallpox
Glanders	Syphilis
Gonococcus infection	Tetanus
Leprosy	Trachoma
Malaria	Trichinosis
Measles	Tuberculosis (all forms)
Meningitis	Typhoid fever
(a) Epidemic cerebrospinal	
(b) Tuberculous	Typhus fever
Mumps	Yellow fever

Of recent years and in certain communities the following have been added:

Tularemia	Endemic typhus
Psittacosis	Influenza
Undulant fever	Encephalitis (acute epidemic)

Many other parasitic and infectious diseases could logically be included in the local lists of communities where such diseases are of particular public health interest, and conversely, some might be excluded because they present no local problem. The point to be decided upon in making a disease notifiable is whether it possesses characteristics which make it dangerous to others beside the individual affected. If it does it enters the responsibilities of those concerned with the maintenance of the health of the herd and must be controlled

With information on prevalence at hand, the Health Authority must act first for the welfare of the community. It cannot be too arbitrary in its procedures because of the danger of arousing undue antagonism, nor can it afford to be too lenient if it is to obtain results due the taxpayers. The principles on which it draws up regulations must rest on a sound understanding of the epidemiology of each disease concerned under the conditions existing at the time

in the particular community. The principles may be indicated in the following categorical questions:

1. Is the disease reported a communicable one of major importance to the community and one which is amenable to control by isolation and/or quarantine?
2. Will isolation of the case prevent further spread from that source?
3. Are contacts with this case probable carriers of the infective agent?
4. Will quarantine of contacts prevent further spread of the disease?
5. What degrees and methods of isolation and quarantine will be most effective and yet interfere the least with the rights of the individual concerned?

These questions can be answered easily in the abstract in regard to most of the communicable diseases. The difficulty comes in applying them to particular cases. The official health inspector and his bureau staff should be given latitude in their authority to temper restrictive measures to the case in point. This does not imply that every health officer may be as strict or lax as he wants, but that under average conditions he may be free to act within the provisions of the law which should be so framed as to admit of intelligent exceptions.

The kind and degree of isolation will depend on the manner in which the infective agent is transmitted. When the causative organism is acquired by direct contact with an infected individual isolation need be no more than is necessary to keep those not directly concerned with the case from contact with it. Attendants will necessarily be obliged to take individual precautions. Diseases transmitted by droplet infection require isolation of the patient behind barriers such as glass or cloth screens, or relative isolation in general hospital wards by separation of beds by a distance which will not be traversed by infected droplets; a matter of 5 feet or more. Screens are advisable even though patients are kept apart. If the agent is a virus which is capable of being carried by the air in a viable condition on droplet nuclei isolation must be strictly limited to an entire room or closed cubicle. Isolation of patients who harbor organisms carried by insects is necessary only to the extent of erecting barriers against the approach of insects to the patient or which will keep insects already on the patient from getting into the general environment.

Where the agent is carried by the alvine discharges or materials from surface lesions, it is only necessary to see that these materials are kept from contaminating others or their food. Personal articles used by the sick should be isolated with the patient when the infective agent is capable of being transmitted by fomites.

In the case of active leprosy and during epidemics of the acute communicable diseases, institutionalization of the patients is frequently necessary or advisable. Open cases of tuberculosis which cannot be safely handled in the home should be placed in institutions, or removed to the care of others who are in a position to attend them under the necessary precautions.

Nursing and other forms of attendance on isolated patients is a matter of extreme importance. A well meaning, sacrificing friend or relative who volunteers to care for a patient but who is unaware of the necessary precautions may undo all of the benefits of the isolation by a single breach of the requirements. For the good of the patient and all concerned a trained attendant is advisable in all serious and important cases.

The use of placards warning of the presence of a communicable disease in a house is justifiable when isolation within the house is not satisfactory or has not been applied quickly enough, and when those who must answer the door are contacts kept in quarantine. This applies only to diseases of such serious nature as smallpox, scarlet fever and diphtheria. At times when the local incidence of a disease threatens to assume epidemic proportions and when it can be assumed that carriers of the disease have not disseminated it to any great extent outside of the limited locality, an entire block of houses or larger geographic units can be isolated from the rest of the community by official guards.

The need for quarantining an individual who is not sick but who has come in contact with one who has an acute communicable disease, or has been exposed in some other way to the infective agent, is frequently a difficult matter to decide. As indicated above the contact may have been made before or after the patient was in the infective stage, and if so, nothing could be gained by placing the contact under quarantine. On the other hand contact may have occurred during the incubation period when the patient was infective but not openly sick. If other conditions justify it such an individual should be quarantined. A known immune who is not a carrier and one who is non-immune and has come in contact with non-carrier immunes but not the patient, need not be quarantined.

During epidemics it may be necessary to close public buildings, theatres, schools and lecture halls to prevent non-immunes from coming into contact with carriers of the infection. It is probable that this should be resorted to more often than it is in the presence of epidemic incidence of some of the acute respiratory and air-borne virus diseases.

The Health Authority should be given the right to restrict the activities of persons engaged in certain occupations when they are found to be carrying pathogenic organisms in a transmissible stage. School teachers with open tuberculosis should not be allowed to

teach, those who are carriers of typhoid organisms and amebæ in their stools should not be given permits as food handlers until their carrier state has been cleared up.

Infective cases of syphilis and gonococcal infections ought not be granted marriage licenses as long as they are capable of transmitting the infection, nor should they be allowed to work as food handlers, barbers, hair-dressers or in any establishment where they may be a menace to others. Prostitutes should be apprehended and given exhaustive tests for infectivity. Children with acute colds, favus, impetigo contagiosa, scabies and pediculosis should be excluded from school until cleared of the infection.

The military services are in an enviable position to restrict the activities of their personnel. The civil authorities might do well to inaugurate some of the practices of the military within their own domain. If they could follow the custom of these services in the control of venereal diseases by regulation of prophylaxis, reporting, and compulsory treatment, it cannot be doubted that the incidence of these diseases could be greatly reduced. The experiences of the armies and navies of the world in the World War are lasting examples of the efficacy of such regulations.

There are a limited number of diseases prevalent in most communities for which there are effective methods of artificial immunization. The Health Authorities in many communities have set up compulsory immunization laws which can be enforced at points where the public comes under their jurisdiction. Compulsory vaccination of children against smallpox before they are permitted entrance to public schools is almost universal, and immunization against diphtheria is well on its way to become so. It may reasonably come with other diseases as quickly as the effectiveness of immunizing agents against them is demonstrated. Private schools, public institutions, industries, and private commercial establishments not infrequently require their personnel to possess vaccination (smallpox) certificates as a prerequisite to continued attendance or employment.

The far-seeing health service of the future may require individuals to submit to such health measures as compulsory pregnancy Wassermann tests, the instillation of silver preparations in the eyes of newborn babies, strict control over abortions, and compulsory Periodic Health Examination of all public employees.

Nuisance ordinances which prohibit persons from spitting in public places and on common carriers, and from defecating and urinating except in authorized conveniences, are personal restrictions enforced by law.

Finally, the Public Health Agencies must always be concerned with the construction and maintenance of institutions at which the public can receive adequate care of conditions which are in any way

communicable. They must build and support public sanatoria for the tuberculous and inaugurate clinics for those with syphilis, tuberculosis and other communicable diseases. They must actively engage in education of the public through their own institutions and offices, and by close coöperation with physicians, social agencies, private concerns, schools, philanthropic institutions and churches which are interested in the same problem.

PROTECTION BY INDIVIDUAL PREVENTIVE MEASURES AND PERSONAL HYGIENE.

The individual can be expected to use ordinary precautions against pathogenic organisms in his environment and to maintain his general state of health at such a level as to enhance his resistance to them.

In most of the preceding discussion the responsibility of the individual to society and himself have been pointed out, and it has been shown that much of the success of the various defensive measures rests on individual understanding and coöperation. In participating in the enforcement of social measures, the individual directly or indirectly protects himself, but many of these efforts are inadequate as ultimate defenses against organisms which are able to filter through the barriers and reach the individual. In spite of public health and general sanitation the individual will always be exposed to organisms against which effective barriers can be erected only by himself.

In the life of the individual the first efforts at personal hygiene must be taken by those on whom he is dependent. The mother who submits to thoroughgoing treatment for syphilis, and the physician or midwife who instils silver salts into the baby's eyes at birth, is practicing personal hygiene on behalf of the infant. So too is the mother who keeps her baby clean by frequent bathing and changing of soiled clothes, and who is particular about the cleanliness of her own nipples and the nursing bottles.

Everything about the baby should be clean within the sanitary meaning of the term. It is not necessary, nor probably even advisable, that everything be sterile, but there should be no clothes put on the baby or food offered it which is grossly contaminated with the ordinary organisms of the environment, or which contain any of the pathogenic organisms. Oral cleanliness should begin at birth to prevent thrush and possibly more serious mouth infections.

Breast-feeding by the mother, or a wetnurse, is always advisable for the first months of life at least, not only for nutritional reasons but because of the passive transfer of immune bodies through breast milk.

Proper nutrition, especially if it is adequate in proteins, vitamins, and salts, probably goes a long way toward keeping up resistance

to infections. Although nothing dogmatic can be said in this regard there are strong indications that at least some of the nutritive elements (vitamin A?) participate in the resistance of tissues to bacterial *invasion, or that their absence from the diet lowers resistance.*

Infant hygiene marks the institution of good habits through training and precept because accustomedness to regular routine care of the body administered by others merges imperceptibly into the acquired habits of the growing pre-school child.

Near the end of the first half of the first year of life the baby should be given the protection of active immunization against diphtheria and smallpox. If at any time during this first year the infant is exposed, or is in danger of exposure to other acute infectious diseases for which passive or active immune agents exist it may be wise, under the particular circumstances of the case, to give this added protection.

The infant should be exposed as little as possible to infectious diseases. The child of tuberculous parents should be removed from this contact if the parents are open cases. It should be carefully guarded from them under all conditions. Promiscuous kissing by nurses, other children and adults in the family, and well-meaning friends should be prohibited within reason. The baby should not be kissed on the mouth. The young baby should not be taken into crowds, especially groups of children.

Cleanliness of the genitalia is essential to prevent ordinary pyogenic infections in both sexes. Precautions should be taken against *gonococcal vaginitis in infant girls. A baby boy with redundant* prepuce should be circumcised.

When a case of an acute contagious disease appears in a household, the baby should be placed in strict isolation and surrounded with all the safe guards of the sick-room.

Should an infant, or one of any other age acquire an acute infection, preventive medicine is immediately concerned with the prevention of complications. Bronchopneumonia, middle-ear disease, sinus infections, meningitis, renal and cardiac complications, are the most to be feared. Intelligent medical care, good nursing, proper *precautions as to overexposure to draughts and chilling, under- or over-feeding, mouth cleanliness, good elimination, rest, and seclusion* are the best safeguards.

Most of the foregoing preventive efforts are applicable to the next four or five years of life. The possibilities of exposure are more frequent, however, because the toddler is moving about within his environment whereas the environment was moving about the infant.

The pre-school child is exposed to infections in its nurse and playmates, and to organisms in and on all kinds of objects which it handles. It ought therefore to be taught the elemental rules of

cleanliness: clean hands at the dining table; no objects to be placed in the mouth; cleanliness after using the toilet; submission to frequent bathing; abstinence from promiscuous kissing; and submission to restrictions in the presence of colds and other minor illnesses.

The pre-school child should receive necessary immunization as early as possible if it had not already done so in infancy.

At this age too the young child should be taught to clean the teeth regularly and properly, to wear shoes as a protection against organisms in the dirt, and to care for minor wounds.

Exposure to tuberculosis at this age should be carefully guarded against. Drastic readjustments in the home may be necessary to accomplish this end but rarely is there no satisfactory solution to the problem. Sentimental attachments are the greatest barriers to be broken down but this can usually be done if tact and sympathy are used rightly, and security can be assured to all concerned.

The grade school child is at the age where certain infectious diseases are more frequent, especially acute rheumatic fever. The "growing pains" of childhood should never be ignored as they may be subclinical evidences of rheumatic infection. This age child is relatively free from serious infections of tuberculosis but a considerable percentage of them already harbor the organism. With present methods of control this cannot be avoided other than by preventing contacts but much can be done to keep it quiescent. Good food, plenty of rest, and good medical care of all inter-current diseases, particularly those of the respiratory tract, are the best precautionary measures known.

All of the good habits of personal cleanliness, elimination, oral and sexual hygiene should be indelibly stamped in the child's pattern of living at this age. What is done out of habit and training now it will do later on the same or rational grounds.

It may be hoped that at all ages after puberty the individual will be open to rational preventive procedures. These are too numerous to consider in detail, but the most important must be reviewed as they constitute in many instances, the first line of defense against invading organisms.

At the outset of the discussion of parasitic disease agents it was shown that the organisms were acquired directly by man through three atria of infection: (1) Alimentary tract; (2) respiratory tract; (3) skin and superficial membranes. It is logical therefore to take up the individual defenses which man can apply deliberately to protect these three channels of infection.

Alimentary Tract Defenses.—In communities where the individual raises little, if any, of his food supply, he should understand that all food brought to him is not necessarily safe even though there are sanitation laws which should protect him. There are always infringements of these laws either through ignorance, accident, or

deliberate evasion. It is necessary therefore that the consumer be aware of the possibilities of infection through his food supply. This can only be accomplished through education. All too frequently the education is by the expensive route of painful experience.

Specifically, milk is always suspect. Unless the consumer can be absolutely assured that the source from which the milk is obtained is sanitary and that the milk is kept clean and safe until delivery he should never use milk without boiling it. All kinds of excuses are given to avoid this. It is claimed that boiling gives it a disagreeable taste, or that it reduces the effectiveness of the vitamins, or makes it less digestible. It may do the first to particular tastes but tastes can be altered. It probably does reduce the activity of vitamin C and possibly vitamin A but no one depends on these sources of vitamins alone today. Boiling does not make milk indigestible.

In general it may be said that the only constantly safe milk is pasteurized milk. This statement is made with the understanding *that the pasteurization, storage and delivery of the milk are also* up to sanitary standard. Grade A certified raw milk may be safe and frequently is but is unreliable over a long time and depends upon too many factors which are difficult to control.

On the farm all milk should be boiled. The fine, fresh milk "right from the cow" looks deliciously clean and appetizing but it may be teeming with harmful organisms.

Condensed, evaporated and tinned whole milk from unbroken cans is sterile when it is opened but readily becomes contaminated by flies, dust, and the fingers if it is not kept under cover and at ice box temperatures. The responsibility for keeping clean milk clean rests on the individual.

Most municipal water supplies are perfectly safe for human consumption. However, after breaks in water mains, floods, and the repair of local plumbing, an individual water supply may become contaminated. In the presence of these and other emergencies all drinking water should be boiled.

The water from springs and wells is as safe as the best water only if it has been demonstrated to be free from pollution from nearby privies, animal pens and surface water flowing into it. The users of such water supplies can have the water tested at intervals by the health departments to make sure that there is no contamination.

Green vegetables may harbor the bacteria of intestinal infections, and typhoid fever, or amebic cysts, if they come from gardens in which these organisms are present in the soil, or if the vegetables are handled by carriers of these infective agents. Under ordinary circumstances these vegetables can be satisfactorily cleaned by washing, scalding or scouring. If for any reason there is any doubt as to their safety the consumer should refrain from eating them

unless they are cooked. The housewife and restaurant proprietor should be expected to see that all connected with the preparation of food are not carriers of the typhoid bacillus or amebic cysts.

Meats and sea foods should be above suspicion before they are consumed. Those concerned must realize that infected meats may show no visible change which will warn them. This is particularly true of pork products which should never be eaten if they have been out of the ice-box for more than a few hours. It is impossible for the buyer of raw meat to be able to determine infection with trichina and other organisms or to know that oysters do not carry typhoid bacilli. The only safe way out of this predicament is to buy from reputable houses and to cook meats thoroughly. Oysters, if sanitary when taken from the bed, chilled immediately and kept chilled until consumed, can be considered safe.

A few infections can be carried into the mouth by articles other than food. If common drinking cups are used very soon after a person with open syphilitic lesions in the mouth or tubercle bacilli in the sputum, these organisms may be transferred to a second party.

Persons with the habit of holding objects in their mouth should break themselves of it. Infections from this source may be rare but they are possible. Every individual should have his own tooth brush. This sounds obvious but it is not uncommon to find several children in a family using a common brush. The greatest danger from this is the transmission of organisms of the normal flora of one mouth to another mouth in which they may be pathogenic: Vincent's organisms, streptococci, staphylococci, pneumococci, etc.

The particular customer will refrain from patronizing restaurants, bars, soft drink stands, and lunch counters where flies are abundant, the waiters are uncleanly, and there is no visible evidence of sanitation of the premises or in washing eating utensils.

The consumer himself may infect his own food. It is not only esthetic but medically important to wash the hands thoroughly before eating, giving particular attention to the nails. Actually the fingers should be kept sanitary at all times, for they are taken to the lips and mouth many times a day independent of the taking of food.

Respiratory Tract Defenses.—The routine hygiene of the nose and throat can hope to do little more than maintain the normal defense mechanisms in a healthy condition. Ordinary cleanliness of the anterior nares and blowing the nose to rid it of accumulated secretion too viscid to drain freely into the naso-pharynx are the only procedures necessary under average conditions. Picking at the nose with dirty fingers and foreign bodies should be avoided because of possible damage to the mucous membrane which may open the way to infection. Exuberant growth of hair in the nose should be cut off if necessary but never plucked out.

It is important that the passage of air through the nose should be unimpeded and that the openings of the sinuses into it be unobstructed. Malformations and deformities which interfere with either of these functions to a harmful degree should be corrected.

Conditions of a non-infectious nature which alter the vascularity and turgescence of the mucous membrane may be important factors in lowering local resistance to invading organisms and may interfere with drainage in the nose itself and the accessory nasal sinuses. Allergic rhinitis, catarrhal conditions brought about by irritating gases and dusts, tobacco smoke, and abrupt changes of temperature are of this nature. Any efforts to prevent these irritations will favor the normal functions of the nasal mucosa and aid in preventing the invasion by potential pathogenic organisms in the flora of the nose or introduced from without.

Sinus infections frequently complicate specific conditions such as the common cold, measles, influenza, and secondary invaders in acute rhinitis of any type so that good medical care is necessary in the treatment of these diseases.

The naso-pharynx is believed to be the portal of entry of the specific agents of poliomyelitis, epidemic encephalitis and leprosy. Meticulous care of the nose and throat is indicated in the presence of these diseases. A particular method of changing the condition of the nasal mucosa to prevent the entrance of the virus of poliomyelitis is given in the Index of Prevention.

The main exchange of respiratory tract organisms between hosts results from their expulsion from the nose and mouth on expiratory droplets. Massive expulsions occur with sneezing and coughing but a few organisms are expelled with ordinary talking and heavy breathing. The burden of prevention of diseases transmitted in this way rests therefore on the host who is careless in these matters. Children should be taught to cover their mouths when they cough or at least to turn their heads, and to sneeze into a handkerchief Everyone can learn that it is obnoxious to talk directly into another's face. Physicians should be particular in examining patients to see that the patient's face is turned away from his, and when he is examining the nose and throat of tuberculous individuals he should protect himself with a mask or a transparent shield between himself and the patient.

In the presence of known infections of a serious nature such as pneumonic plague and epidemic influenza all who are in attendance on the sick or are brought into close proximity with them should wear masks. A simple mask may be made of four or more folds of surgical absorbent gauze cut large enough to cover the face from the bridge of the nose to the chin and extend laterally over the cheeks. It is held in place by tapes sewed to all four corners, those from the upper two being carried back and upward to be tied over the top

of the head and the lower tapes drawn tight beneath the occiput and tied. These masks become damp and heavily contaminated after a few hours and should be changed frequently. No one should ever use another's mask unless it has been sterilized by boiling or steam.

The person with an acute respiratory infection should not mingle with crowds for the sake of others, and conversely it is wise to avoid unnecessary crowds during periods of high incidence of colds, influenza, measles, pneumonia, poliomyelitis and other air-borne infectious diseases.

Skin and Superficial Mucous Membrane Defenses.—The whole body surface should be bathed frequently to remove dead epithelium, inspissated sebum, salt crystals from sweat and accumulated foreign matter. Bathing also improves the circulation in the skin by causing capillary contraction and dilatation which aids in forcing the movement of static tissue fluids. It also opens the mouths of sweat and oil glands and hair follicles thus preventing the accumulation of their secretions which favors bacterial growth.

A reasonable amount of soap enhances the removal of natural oil deposits on the skin and greases from extraneous sources. The too liberal use of alkaline soap is inadvisable in infants and during warm weather because it removes more than the desired amount of protecting oils.

General body cleanliness is the best preventive against the pyodermias, fungus infections and ectoparasites, and probably plays an important part in the prophylaxis of such conditions as leprosy, blastomycosis, hookworm disease, impetigo, anthrax, and many other infections of the skin and general diseases caused by organisms which enter through it.

Whenever the continuity of the skin is broken or the surface cells are devitalized an opportunity is given for the entrance of organisms which are members of the normal flora of the skin or for exotic organisms which gain access to it. The break may be minute and undemonstrable but to organisms such as the streptococcus of erysipelas it is a wide open breach. No wound can be too small to ignore.

Larger lesions such as abrasions, blisters, burns, contusions, lacerations and puncture wounds are highly vulnerable points for the entrance of pathogenic organisms. Some bacteria are present in every wound. Their ability to produce clinical infection depends on their number, virulence and the resistance of the host. To prevent outward infection in all wounds the number of organisms must be reduced. There is no more effective method of accomplishing this than the liberal use of soap and water, gently but thoroughly applied. The use of secondary antiseptics is desirable to prevent the multiplication of bacteria which remain in the wound. The par-

ticular antiseptic is unfortunately still a matter of opinion in the choice of one of several effective bacteriostatic materials. (See Disinfection and Antisepsis, page 585.)

Devitalized tissues should be cut away from all wounds and the interior of puncture wounds should be made accessible to air to prevent the growth of anaerobic bacteria, particularly *C. tetani* and the gas infection organisms. Wounds caused by gunpowder burns, crushing wounds and punctures by nails, splinters, etc., which have been acquired out of doors are particularly liable to be contaminated with clostridia. Active immunization against tetanus by the prophylactic use of tetanus toxoid is receiving increasing support as a useful measure.

Surgical technics are in great part the application of effective preventive measures against infection. With the realization that deliberate surface incisions must pass through a skin that cannot be completely sterilized and that the hands of the operator cannot be made bacteria free a highly specialized routine has been developed whereby the possibilities of bacterial contamination of the operative wound have been reduced to the minimum. The reader must be referred to standard works on operative surgery for the details of these refined methods of prophylaxis.

The prevention of infection of the eyes and their associated structures involves general maintenance of their normal functions by avoiding eye strain, contamination from dirty fingers and other objects, the use of goggles in contaminated atmospheres, and when the eyes are exposed to irritating bright lights, prophylactic eye-washes following removal of foreign bodies in the conjunctival sac, care of the lids from irritating substances, caution in cosmetic procedure such as the plucking of eyebrows and eyelashes, and immediate attention to injuries in and about the eyes.

The prevention of ear infection divides itself into two main aspects: (1) Infections through and in the external auditory canal; (2) ascending infections by way of the Eustachian tube.

The contour of the external auditory canal favors the accumulation of natural secretions and dust and dirt from the outside. If the outer portions beyond the protecting hairs are not kept clear of these materials the normal cerumen and other secretions behind it are unable to remove themselves spontaneously. This may result in irritation and devitalization of the lining cells of the canal and favor infection. The use of hard, picking instruments to remove cerumen and scratch the ear is deplored because of the danger of injury and secondary infection. Children should be watched for the presence of foreign bodies in the ears as their presence predisposes to infection.

Extension of infection up the Eustachian tube is a common accompaniment of inflammatory conditions in the naso-pharynx.

When to this is added congestion and closure of the internal orifice the mucous secretions and bacteria accumulate and predispose to the production of otitis media. This is particularly true in measles, the common cold, septic throat infections and scarlet fever. There are indications that removal of adenoids acts to prevent these possibilities. Oral hygiene in general reduces the danger, or at least the extent of such involvement. Mild washes and gargles are therefore recommended in acute upper respiratory infections, not so much because they in any way sterilize the parts but remove accumulated secretions. In this connection, strong, too often repeated gargling may do more harm than good by forcing materials from the throat into the Eustachian tube. Forcible blowing of the nose with both nares and the mouth closed simultaneously is harmful for the same reason.

The female genital tract is open to infection from many sources and there are a large number of predisposing causes which contribute to it.

The young prepuberty girl is subject to gonococcal vulvo-vaginitis because the vaginal mucosa is thin and non-resistant. Precautions should be taken in households where hygienic conditions are poor to see that gonococci are not transferred from other members by means of fingers and contaminated clothing, bed covers, towels and wash cloths. In better ordered homes the same danger exists by transfer of infection from nurses and maids and child companions. In institutions every little girl should have her individual linen and toilet articles and should be taught the fundamentals of genital cleanliness.

With the onset of menstruation the genital tract opens up and is subject to periodic physiologic changes in the mucous membranes and their secretions. During the flow of uterine secretions the lower genital tract becomes more alkaline and favorable to bacterial growth. Feminine hygiene demands more particular attention therefore during and after the menstrual period.

The non-virginal genital canal is subject to invasion by gonococci, spirochetes, protozoa and all of the more common pyogenic organisms. They gain entrance through coitus, the introduction of foreign bodies, manipulation, the use of unclean instruments during childbirth and the performance of abortions, by extension from the adnexa, and from violence and other forms of traumatism.

The prevention of these infections can be accomplished only by attention to the particular mechanisms involved; the venereal diseases by every channel of approach to this broad problem; restriction of abortion to the practice of licensed physicians who can operate under surgical technic; education of physicians in the proper conduct of childbirth and care of the puerperal woman; medical intervention in the presence of infections elsewhere which might

extend to the genital tract; the instruction of the woman in the use of douches; and the immediate attention to wounds and injuries of all kinds by a qualified physician.

In the male it is almost entirely a question of sex hygiene. General cleanliness of the external genitalia is essential at all times to prevent non-specific balanitis, phimosis, and soft chancre. Venereal disease prophylaxis is outlined on page 607.

In both sexes education in sex hygiene will always be the only sound basis for venereal disease prophylaxis. Because this involves attitudes and ideals as well as practical methods to avoid the harmful results of bad sex hygiene other than the contraction of venereal disease, this whole subject will be discussed under Psychobiologic and Biosocial Influences on page 664.

PROTECTION BY SPECIFIC IMMUNIZING MEASURES.

The basis of all artificial immunization rests on the fact that antibodies against specific antigens can be produced in the body of a susceptible individual by means other than the processes of natural infection.

The mechanisms involved in immunity in general have been thoroughly reviewed in a previous section without reference to whether the antigen was introduced under natural conditions or artificially. The present discussion is limited to those attempts to produce immunity by the deliberate introduction of antigenic substances into the body or the administration of preformed antibodies.

The idea still exists in many quarters that children should be permitted to contract some of the exanthemata when they are young because, as they say, they will get them anyway, so why not early. The author wishes to add his unqualified objection to this archiac conception. No one can endorse such an idea who is at all conversant with the mortalities resulting from the so-called harmless childhood diseases and who knows the serious complications, defects and disabilities which they frequently leave in their wake.

Instead, every effort should be made to protect the young and all other ages from these infections. Artificial immunization is rapidly becoming the solution of the problem for many of them.

In order to apply the principles of protective immunization there must be available either: (1) A specific antigen of effective potency; (2) a lower animal in which a specific antibody of satisfactory potency can be produced; or (3) human serum containing adequate amounts of the specific antibody.

When a specific antigen is available either as a whole organism, alive but attenuated, or dead, or as a specific fraction of the organism, this antigen may be introduced parenterally (and probably

per os in limited instances) into a susceptible non-immune with the intention of stimulating formation of specific antibodies against it which will be protective against subsequent natural invasion by the same organism. Such active artificial immunization has been accomplished in the diseases considered below. Only those which are effective as prophylactic measures are discussed.

1. **Active Immunization by Specific Antigens.**—The immunizing agent, if a virulent bacterium, can be made suitable for use by attenuation through prolonged cultivation on artificial media or at temperatures above that of ordinary cultivation; by passage through a series of animals of the same species; and by cultivation in the presence of weak antiseptics. Viruses may be attenuated by passage through animals of another species.

Active immunization by means of killed organisms is of use in those instances where protection is desired against intracellular toxins.

Bacterial products, particularly the soluble exotoxins, can be obtained from killed cultures or organisms which produce such toxins or by the use of filtrates from the culture media on which the organisms were grown These toxins can be further modified by chemical means to make them non-toxic to the human without loss of their antigenic powers.

The preparations made for immunization by these means are known as vaccines, toxins, and a number of modified toxins known as toxoids or anatoxin.

(a) **Prophylactic Vaccines of Living Attenuated Bacteria.**—*Plague.*—Organisms from a three-year-old laboratory were subsequently cultivated by Strong at a temperature above 41° C. They are reported to be avirulent for monkeys and guinea-pigs but to retain their antigenic properties for man. The possibility of danger from these organisms has not been thoroughly ruled out.

Tuberculosis.—An attenuated human strain of *Bacillus tuberculosis* obtained through 230 generations on a medium of 5 per cent glycerin potato saturated with beef bile.

It is avirulent for laboratory animals. There is no incontrovertible proof that this strain may not revert to the virulent form.

It is administered by mouth to infants and children, and is known as Bacillus Calmette-Guerin (B.C.G.).

Cholera.—Haffkine's vaccine was formerly obtained by cultures of the cholera vibrio at temperatures above 40° C. Subsequent investigation showed that passage through guinea-pigs gave an effective, safe attenuation without resort to cultivation at high temperatures.

(b) **Prophylactic Vaccines of Killed Organisms.**—*Typhoid, Paratyphoid A and B.*—Eighteen-hour agar cultures of the "Rawlings" strain are washed off with sterile bouillon so that the suspensions

contain approximately one billion organisms per cubic centimeter. The suspension is heated to 53° C. for one hour which kills all the organisms. Tricresol 0.25 per cent is added to prevent contamination.

"Triple vaccine" is made of suspensions of organisms of *B. paratyphosus A* (*S. paratyphi*) and *B. paratyphosus B.* (*S. schottmülleri*) grown in the same way and combined with a suspension of *E. typhi* in the proportions of 300,000,000 of each of the paratyphoid organisms to 500,000,000 of *E. typhi.*

Typhoid vaccine and triple vaccine are administered in doses of 500,000,000 to 1,000,000,000 of the typhoid organisms at intervals of a week or ten days for three successive doses.

A satisfactory immunity probably does not last on an average more than two years.

Vaccine in ox-bile, administered by mouth in capsules, is used extensively in Europe and South Africa with apparently good results. It is believed to produce a local immunity of the intestinal mucosa.

Cholera.—The vaccine of choice for cholera is obtained from heat or carbolic acid killed cholera vibrios grown on agar or broth. The Pasteur Institute vaccine is a broth culture killed by heat at 50° C. Growths from agar, suspended in salt solution may be killed by heating at 56° C. for one hour and adding 0.5 per cent carbolic acid. The vaccine is administered in doses of 1,000,000,000 cholera vibrios at intervals of five to seven days for two or three doses. Immunity is effective for approximately two years.

It may be combined with triple vaccine (Castellani's T. A. B. C.) in amounts to contain 500,000,000 *E. typhi,* 250,000,000 each of *B. paratyphosus A* and *paratyphosus B* and 2,000,000,000 cholera vibrios. Dose: One-half cubic centimeter at the first dose followed by 1 cc. one week later. A third dose of 0.5 cc. may be given if desired, two weeks after the first injection. Injections should be made into loose tissues.

Plague.—Haffkine's vaccine is prepared from a four or six weeks' growth of *P. pestis* in broth killed by sterilization at 65° to 70° C. for one hour. Carbolic acid may be added as a preservative. The vaccine is administered subcutaneously in a single dose of 3 cc. for an adult male.

The vaccine recommended and used by the German Plague Commission was a suspension in normal saline of organisms grown on agar and killed by heating at 65° C.

A protective immunity lasts for only a few months at best.

Typhus and Other Rickettsias.—Weigl[1] has succeeded in infecting large numbers of lice with typhus organisms and then triturating their intestines with weak carbolic acid solution. Mexican typhus

[1] Weigl Med. Klin., 20, 1046, 1924.

organisms can be obtained in large numbers from the peritoneal cavities of infected rats. Zinsser and Castaneda made formalinized suspensions of the organisms and obtained immunization of guinea-pigs against the Mexican disease and 30 per cent immunity against the European strain. No conclusive results have yet been obtained in man.

A vaccine has been prepared against the organism of Rocky Mountain spotted fever from ground-up infected ticks. There is no evidence that the rickettsiæ are alive in the completed vaccine.

Parker and Davis[1] used this vaccine as a prophylactic among sheep herders in a heavily infected region in Montana and for laboratory workers. Ten years' experience with it has impressed Parker with its probable value, not so much as a real prophylactic against infection but as an active agent which minimizes the disease in those who acquire it. This, he believes, is apparently so in those who have received more than one immunizing treatment over several seasons.

Bengston[2] has obtained significant results in the protection of guinea-pigs against lethal doses of rickettsiæ by the use of a formolized vaccine of Rocky Mountain spotted fever rickettsiæ grown on a modified Maitland medium. Reports seem to indicate that this may be superior to vaccine made from ground-up infected ticks.

Pertussis.—Sauer's vaccine contains 10,000,000,000 *H. pertussis* per cubic centimeter of vaccine. The organisms are grown on Bordet's medium enriched with freshly defibrinated human blood and then killed by 0.5 per cent phenol at refrigerator temperature for one week. The organisms were in the virulent smooth hemolytic phase.

The dose of the vaccine for a child is 7 or 8 cc. given over a period of several weeks in weekly injections of 1 or 1.5 cc. per dose.

The vaccine should be administered as long before exposure as possible, preferably a matter of months.

Pneumococcus Infections.—Successful vaccines have been obtained against Type I and Type II pneumococcus. The organisms are washed off the medium with salt solution and killed at 56° C. for one-half hour. Tricresol 0.3 per cent is added as preservative. Each cubic centimeter of the vaccine contains 1,000,000,000 pneumococci.

The vaccine is administered in three doses at weekly intervals; first dose 3,000,000,000, second dose 6,000,000,000, third dose 9,000,000,000 organisms.

Rabies.—A vaccine which probably contains killed rabies virus has been developed by Semple. It consists of 8 per cent mixture of virus brain in saline solution in which the virus is killed by the

[1] Parker, R. R., and Davis, G. E. U. S. Pub. Health Rep., 48, 839, 1933.
[2] Bengston, I. A. Pub. Health Rep., U. S. Pub. Health Serv., 52, 1696, 1937.

addition of 1 per cent phenol and incubating at 37° C. for twenty-four hours. This is then diluted to 4 per cent virus brain and 0.5 per cent phenol by adding an equal amount of saline solution.

It is administered in doses of 2 to 3 cc. daily for fourteen or more days.

Staphylococcus Infections.—Stock or autogenous vaccines made from agar cultures in suspension in saline. The organisms are killed by heat at 60° C. for one-half to one hour. The suspension is standardized by nephelometer or counting chamber to contain approximately 500,000,000 organisms per cubic centimeter.

It is administered in bi-weekly or weekly doses of 0.5 to 1 cc. each.

(*c*) **Prophylactic Vaccines of Unaltered Bacterial Products.**—*Cholera.*—Cholera vibrios are grown by Strong on agar and washed off in salt solution. The organisms are then killed by heat at 60° C. The suspension is allowed to stand at incubation temperature for five days and then passed through a Berkefeld candle filter. The sterile filtrate is used for inoculation.

Scarlet Fever.—Scarlet fever toxin is obtained from mixed strains of streptococci (Dochez NY5 and Dick II) grown on meat infusion-peptone broths and Douglas' tryptic digest broth at 37° C. for seven days. The broth is phenolized with 0.5 per cent phenol and the organisms removed by filtration through a Berkefeld candle. The strength of the filtrate is standardized in animal skin-test doses (S.T.D.).

Immunization is produced by the subcutaneous or intramuscular injection of the toxin in weekly doses of increasing amounts of S.T.D. First week 500 S.T.D., second week 2000 S.T.D., third week 6000 S.T.D. and fourth week 12000 S.T.D.

Pertussis.—An unaltered antigenic extract of *H. pertussis* which may eventually prove to be efficacious has been obtained by Krueger by grinding Phase I organisms in Locke's solution and filtering through a collodion membrane. The filtrate is strongly antigenic in animals and is non-toxic.

(*d*) **Prophylactic Vaccines of Treated Bacterial Products.**—*Diphtheria.*—If normal diphtheria toxin is treated with formaldehyde and incubated it loses its toxicity but retains its antigenic powers as demonstrated by antitoxin in the blood and flocculation *in vitro.* This changed toxin is called *anatoxin* by Ramon in Europe and *toxoid* in this country. Toxoid is administered in two doses of 1 cc. each at an interval of one week. It requires five or more months to produce its maximum titre of antitoxin. Toxoid contains no horse serum and is therefore not sensitizing to it. On the other hand the bacterial proteins may produce some reaction in susceptible individuals, usually adults and older children.

Diphtheria toxoid treated with alum loses much of the sensitizing powers due to bacterial protein and is believed by its supporters to

produce a longer immunity. This *alum precipitated toxoid* as it is called is administered in a single dose of 1 cc. Its advantages over *toxoid* as measured by percentage of Schick positives who become Schick negative under its influence has not been completely demonstrated as yet.

Tetanus.—Tetanus toxin treated with 0.3 per cent formalin and incubated at 37° C. for four to six weeks loses its toxicity but retains its antigenic powers. This *tetanus anatoxin* or *toxoid* is administered as a long-time immunizing agent against possible infection with the tetanus bacillus. It is given in two doses of 1 cc. each two months apart.

Staphylococcic Infection.—Toxoid has been developed from staphylococcus toxin by treatment with formalin. It has been shown to raise the antitoxin titre of the blood against staphylococci in individuals in whom the titre was low.

(c) Prophylactic Vaccines of Attenuated and Inactivated Filterable Viruses.—*Smallpox.*—If the virus from a human case of smallpox is inoculated into a calf it produces lesions in that animal from which virus can again be obtained. The virus, however, has become so attenuated by the animal passage as to produce only a local lesion in most instances when re-inoculated into the skin of man. The attenuated virus is the *vaccine* of Jenner which is used throughout the world in the control of smallpox.

Vaccine is obtained by scraping the lesions of the calf and adding to this material four times its weight of glycerin 50 parts, water 49 parts and carbolic acid 1 part. After this mixture has been allowed to stand for three or four weeks to permit time for all bacteria present to die out the glycerinated pulp is triturated thoroughly and is then ready for use.

Pulp is put up in capillary tubes or allowed to dry on bone or ivory "points" as dry virus.

Smallpox vaccine should be thoroughly tested for sterility by plating and for tetanus bacilli by mouse inoculation before it is distributed. The virus will remain potent for five months if kept cool.

Vaccination is performed by placing a single drop of vaccine on cleansed skin and making a fine scratch through it of not more than $\frac{1}{8}$ *inch in length. The virus is then massaged into the scratch for* fifteen seconds with the side of the vaccinating needle or a sterile toothpick. The scarification should not have drawn blood. The multiple pressure method consists in placing a drop of vaccine on cleansed skin and then pressing the pointed end of a sterile needle against the skin through the drop in such a way that the point of the needle depresses the skin slightly but does not visibly puncture it. This pressure is repeated rapidly thirty times, the point of the needle never covering an area more than $\frac{1}{8}$ inch in diameter. The excess virus is wiped off and the vaccination is left uncovered.

There are four types of reaction to smallpox vaccine:

1. The primary "take" or vaccinia characterized by the formation of a typical smallpox papule on the third to fifth day with vesiculation at its height on the eleventh to fifteenth days. It occurs in the non-immunes.

2. Accelerated vaccinoid reaction shows papule formation on the third or fourth day, vesiculation by the fifth and rapid subsidence thereafter, usually without pustule formation. This is the reaction of the partial immunes.

3. Immediate reaction shows a papule within forty-eight hours and immediate subsidence without vesicle or pustule. It occurs in individuals with high immunity.

4. No reaction or a papule forming after seventy-two hours without any further progression is evidence that the virus had lost its potency or the technic of vaccination was faulty. It should be repeated.

The duration of vaccination immunity is five to seven years. Vaccination should be compulsory in infancy and every seven years thereafter for at least the first three decades of life.

Rabies.—The virus of rabid animals or "street virus" is inoculated into a series of 21 to 30 rabbits in which it becomes fixed in the nervous tissue as *virus fixe.*

The medulla of a rabbit containing *virus fixe* is then emulsified in sterile salt solution and injected into the brain or subdural space of another rabbit. When this rabbit dies its cord is removed immediately under strict precautions and hung by a thread in a tall bottle with a few pieces of potassium hydrate in the bottom. The suspended cord gradually dries under these conditions and the virus becomes progressively attenuated. Cords of one to eight days are used for prophylactic immunization. For use 1 cm. of cord is emulsified in 3 cc. of sterile salt solution or 5 cc. of bouillon. The amount of each to be used varies with the age of the cord.

Immunization is performed by daily injections of cord emulsions of different ages for twenty-one successive days.

For adults, 2 injections a day of eight-, seven- or six-day cord in doses of 3 cc. each are given for the first two days and four- or five-day cords on the third day. One injection of 2 cc. per day of cords three, four or five days of age are then given for the remaining eighteen days.

Högyes' modification uses varying dilutions of fixed virus cords ground up and diluted with salt solution. The first injection of 3 cc. is with a dilution of 1 to 10,000. This dilution is gradually decreased on successive days until the last dilution is 1 to 100.

Harris further modified the dried cord technic by freezing fixed virus with CO_2 snow and drying it rapidly *in vacuo* over sulphuric acid. This keeps several months on ice in the dark and from it vaccines of constant strength are prepared as needed.

The use of rabies vaccine prophylactically is practically limited to individuals who have been bitten by an animal which is rabid or suspected of being so.

Yellow Fever.—Hindle[1] has reported experimental success in the immunization of mice and monkeys with attenuated yellow fever virus.

Poliomyelitis.—Active prophylactic immunization of monkeys with attenuated (ricinoleated)[2] poliomyelitis virus has been accomplished but the application of this to prevention in man awaits further developments. Monkey passage virus is attenuated to a degree that makes it possible that active virus obtained in this way might be available for human use.

2. Passive Immunization by Preformed Antibodies.—Immune antibodies may be obtained from the serum of patients convalescent from some of the bacterial and virus diseases or from individuals possessing such antibodies from previous infections or produced by immunizing agents. The sera of lower animals which contain antibodies produced in them by active immunization may also be used. The latter are largely of the nature of antitoxins. Animal sera and the antibodies in human serum may also be anti-invasive.

(*a*) **Immune Sera Obtained From Human Sources.**—*Measles.*—The serum of convalescents from measles and measles-immune adults in doses of 3 to 15 cc. will confer a passive incomplete immunity upon a child who has been exposed to an active case.

Whole blood from a compatible donor may be injected immediately intramuscularly. It must be used within five days after exposure. The immunity lasts from two weeks to a month.

Poliomyelitis.—The presence of immune antibodies in post-poliomyelitic and normal adult serum theoretically should indicate that such serum might be a possible passive prophylactic immunizing agent during epidemic exposures to the disease. Experience with it has been conflicting, largely because of lack of statistical control.

Yellow Fever.—The serum of an individual who has had an attack of yellow fever possesses antibodies which can be utilized to produce passive prophylactic immunity in another. Although the full value of immune serum has not been demonstrated it is likely that such degree of protection as it affords will be of value during epidemics.

Pertussis.—Human adult immune serum is reported by Jundell[3] to have produced favorable results in reducing the severity of whooping cough in exposed children. He succeeded in getting these results only after augmenting the adult titre by preliminary injections of pertussis vaccine.

[1] Hindle, E.: Brit. Med. Jour., 1, 976, 1928.
[2] Brodie, M.: Am. Jour. Pub. Health, 25, 54, 1935, Kolmer, J. Ibid., 26, 149, 1936.
[3] Jundell, I.: Acta Pædiat., 16, 1, 1933.

Debré reports some success with convalescent serum (Gay).

(*b*) **Immune Antibodies Obtained From Animal Sources.**—*Diphtheria.*—The use of antitoxic horse serum may be used as a prophylaxis in contact cases. It is administered subcutaneously in doses of 500 to 1000 units. The passive immunity is short-lived.

Plague.—Antitoxic and possibly antibacterial animal plague serums are mildly protective but difficult to obtain and standardize. They have not been perfected to the point of reliability as a protective measure.

Tetanus.—The serum from horses which have been made hyperimmune to tetanus toxin is obtained by bleeding from the jugular vein and preserving with 0.5 per cent carbolic acid or 0.4 per cent tricresol.

The antitoxic content is standardized to antitoxin units, one unit being ten times the least amount of serum necessary to save the life of a 350-gram guinea-pig for ninety-six hours against a standard test dose of 100 minimal lethal doses of a standard precipitated toxin.

Prophylactic tetanus antitoxic serum is administered subcutaneously in amounts of not less than 1500 units.

The antitoxin remains in the body for only about two weeks so that as a prophylactic in severe injuries and those where the likelihood of tetanus is great a second injection should be given within a week after the first. The presence of foreign serum proteins in antitetanic serum makes it essential to take strict precautions against anaphylaxis.

Clostridium welchii Infection.—A hyperimmunity to *C. welchii* toxins can be produced in horses and mules. The serum of these animals, which is antitoxic, is obtained and standardized so that 1 cc. contains 1 unit, or the amount which will neutralize 1000 M.L.D. of *C. welchii* toxin.

Clostridium œdematis-maligni Infection.—An antitoxic serum can be obtained from horses made hyperimmune by injections of the toxin. It has not been definitely standardized and is usually combined in a polyvalent serum with *C. welchii* and *C. tetani.*

The antitoxins against the anaërobic gas-producing organisms of wound infection find their greatest usefulness in the injuries of war.

Scarlet Fever.—Immune horse serum containing *Streptococcus scarlatinæ* antitoxin is standardized in units, each unit of antitoxin being the smallest amount which neutralizes 50 S.T.D. of scarlatinal streptococcus toxin.

Prophylactic immunization of contact cases in the period of incubation has been used with varying degrees of success. It should probably be repeated more than once but allowance must be made for the dangers of anaphylaxis.

3. **Combined Antigen-antibody Prophylactic Immunization.**—The simultaneous administration of toxins and antitoxins has the advantage in some instances of producing an immediate passive immunity and a delayed active immunization. The use of an antibody mixture along with a powerful antigen also reduces the toxicity of the latter. Toxin-antitoxin mixtures have almost entirely superseded the use of plain vaccines in some few diseases.

Diphtheria.—Toxin-antitoxin prophylaxis in diphtheria was the best available preventive before the perfection of toxoid. It is still used by many when undesirable reactions to toxoid are to be avoided in adults and older children.

The amounts of toxin and antitoxin used are regulated so that there is a sufficient quantity of free toxin to be effective in producing active immunity. The standard balanced mixture of the New York Department of Health contains 0.1L + of toxin with about 0.08 unit of antitoxin.

The small amount of horse serum in the antitoxin component may produce some sensitization in susceptible individuals.

Toxin-antitoxin is administered intramuscularly or subcutaneously in three doses of 1 cc each at weekly intervals. The maximum immunity is reached in three to five months. If a child who has been inoculated fails to become Schick negative within six months an attempt at immunization should be repeated with the same or another form of vaccine.

Yellow Fever.—Sawyer[1] and his co-workers have demonstrated experimentally that monkeys and mice can be immunized by immune serum-virus mixtures.

The results in man are impressive but await further development.

Typhus.—A sero-vaccine in which the virus is neutralized by immune or convalescent serum was suggested by DaRocha Lima and in the hands of Zinsser and Batchelder[2] produced an active immunity in guinea-pigs.

Dysentery.—If dysentery bacilli and the corresponding antiserum are placed together *in vitro* the sensitizers in the serum unite with the bacterial cells. When the excess serum has been removed, the remaining bacteria (killed) and their attached antibodies is known as a *sensitized vaccine.*

Such a vaccine produces a grade of immunity superior to that of a vaccine from unaltered organisms. There is some question as to whether the antibodies confer some passive immunity as claimed by Besredka.

Poliomyelitis.—Brodie[3] and Brodie and Goldbloom[4] report experi-

[1] Sawyer, W. A., Kitchen, S. F., and Lloyd, W.. Proc Soc Exper Biol and Med., 29, 62, 1931

[2] Zinsser, H., and Batchelder, Jour Exper. Med., 51, 847, 1930

[3] Brodie, M.: Jour. Exper Med., 56, 493, 1932

[4] Brodie, M., and Goldbloom, A Jour. Exper Med., 53, 885, 1931.

mental work on combinations of poliomyelitis immune serum and virus given together in an incubated mixture or separately. He obtained the best immunity in monkeys when the serum was administered with or after the virus. The immunity was generally *less than that produced by monkey-passage virus alone.* The serum-virus combination has not been tried in man.

PROTECTION BY DISINFECTION AND ANTISEPSIS.

Disinfection is the destruction of pathogenic organisms. The difference between disinfection and *sterilization* is a matter of degree, the latter destroying all forms of life on a contaminated object. *Antisepsis* is the inhibition of the growth of microscopic organisms and antiseptics are therefore *bacteriostatic agents.* They may or may not sterilize. A *germicide* is a particular type of disinfectant which destroys germs or bacteria (*bactericide*).

In the prevention of disease, disinfectants and antiseptics are useful because they destroy or modify the activities of infective and parasitic agents within or on the host and so prevent their dissemination in the environment or to other hosts, or act on these *agents in the environment and prevent their acquisition* by new hosts.

The use of the principles is limited by the ubiquity of many parasites and the practical impossibility of removing them altogether from the environment. They are most useful in destroying organisms in and on man and on objects with which he comes in close contact.

There are a number of natural agents which are unfavorable to living organisms. They include heat, desiccation, light rays, and cold. The present concern, however, is with artificial methods of disinfection and bacteriostasis.

Soap and water removes and destroys the great majority of organisms from the surface of the human body and from most objects which can be washed. It is the most universally used disinfectant and is relied upon most largely in the application of the general principle of cleanliness. When applied to the human body it prevents the acquisition of parasites from the environment and reduces the possibilities of autoinfection of wounds and mucous membranes. It is the outstanding means of preventing the contamination of food by food handlers. Soap and water cleansing of all objects in the sick-room is the most effective method of terminal disinfection and is of more value than chemical disinfection.

Disinfection of the alvine discharges (feces and urine) is required whenever there is no adequate, safe disposal system available, and when in known cases of sickness due to organisms discharged in these materials, the discharges must be handled by others in disposing of them.

Owing to the bulk of organic matter in feces and the slowness of penetration to the interior of the mass the disinfectant must be well mixed with it and allowed to remain in contact for a sufficient length of time. The most commonly used and cheapest disinfectant for this purpose is compound cresol solution (Liquor cresolis compositus). Equal volumes of the solution and the excreta are thoroughly mixed and allowed to stand for one hour. Formalin, 10 per cent solution, phenol, 5 per cent solution and chlorinated lime, 3 per cent solution may be used in the same way as the above.

For the destruction of helminth eggs Stiles recommends making a 3 per cent solution of sodium hydroxide in the feces. Protozoan cysts can be killed in the same way.

The materials accumulated in sputum cups can be disinfected by adding equal amounts of any of the disinfectants used on feces. A small amount of compound cresol solution in the bottom of the sputum cup will disinfect sputum as it is discharged.

Soiled bed-linen and sleeping clothes may be disinfected before laundering by soaking for one hour in 3 per cent chlorinated lime or cresol compound.

Germicides are used to destroy bacteria on the skin and for the sterilization of objects which are brought into intimate contact with the skin and mucous membranes. They are useful therefore for pre-operative preparations of the hands and other parts of the body and in the sterilization of operating and examining instruments, combs, brushes, razors, hair tweezers, and articles of clothing such as shoes, belts, and other materials not subject to laundering.

The most generally used germicide for sterilizing common articles is bichloride of mercury in 1 to 1000 solution in water. Alcohol is also commonly employed and acetone and ether may be used unless contraindicated. Dichloramine-T is highly satisfactory. Carbolic acid 5 per cent and formalin 10 per cent in water are widely used as such or as commercial preparations of them.

A 1 or 2 per cent solution of salicylic acid in alcohol is effective in killing fungi in shoes and slippers. This strength may be safely poured on the stocking while it is on the foot in sufficient amount to soak it thoroughly, and then the shoe or slipper to be cleaned is worn over it throughout the day.

There are a number of disinfectants which have particular applications:

Lye, or sodium hydroxide is especially advantageous for disinfecting barns and stables against *Brucella abortus.*

Silver nitrate 1 per cent is used as Credé's prophylactic against ophthalmia neonatorum. Argyrol, 25 per cent solution and protargol, 3 per cent solution are silver preparations which can replace the nitrate.

Copper sulphate in 1 part per 1,000,000 of water will kill many species of algæ.

Betanaphthol is used medicinally as an intestinal antiseptic.

Napthalene or tar camphor is effective against many vermin and fungi.

Potassium permanganate is weakly germicidal and is used in surgical antisepsis and for the sterilization of well water.

Lime (CaO) and calcium hydroxide, 1 per cent watery solution, kill non-spore-bearing bacteria in a few hours. Three per cent solution kills *E. typhi* in one hour. Milk of lime (slacked lime in 4 to 8 volumes of water) is used to disinfect privies and other filth contaminated premises.

Chlorinated lime or bleaching powder in 4 per cent solution in water is used to disinfect excreta. It is used also in the purification of water.

Labarraque's solution (Liquor sodiæ chlorinatæ) is used for skin cleansing in dilution of 1 to 4 with water.

Antiseptics are employed prophylactically to inhibit bacterial growth on the skin and mucous membranes especially when these tissues are known to be contaminated, or when they have been opened to invasion by pathogenic organisms by wounds and injuries.

Except in the conjunctiva, all chemical antiseptics should be preceded by a thorough but gentle cleansing with soap and water. The particular prophylactic antiseptic to be used will depend on its availability and the judgment of the user. There are many on the market, a few only of which have outstanding merits. Allen, Moorhead and Edgerly[1] have the following to say about the use of antiseptics. "Often the physician who uses the several available antiseptic products is at fault in his application of the preparation. This may be the cause of many of the unfavorable results noted in connection with the use of some of the antiseptics in common usage today. He must first understand the active, dynamic, pathologic processes at which his medication is directed. Even with the understanding of the problem at hand, he may and often does do more harm by medication of the wound than all the germs present would do under ordinary circumstances. Through the use of too strong, or too often applied antiseptics he may destroy living and reparative tissues, thereby producing delayed healing of the ulcerated area, an unnecessary slough, or even systemic reactions following the absorption of toxic products of tissue degeneration. An agent which kills or inhibits bacteria present in the wound, but does not at the same time destroy tissue, nor interfere with the natural body defensive mechanisms is far more desirable than one which kills all the organisms present and at the same time accomplishes the destruction of the tissues with which it comes into contact.

"An infection occurs only when the contaminants, present in every wound, are in sufficiently large numbers, or of sufficient virulence to overcome the local defensive processes. Therefore, a

[1] Allen, A. W., Moorhead, J. J., and Edgerly, M. P.: Am. Jour. Surg., 23, 371, 1934.

mechanical cleansing of the locally contaminated, or later infected area, and the judicious application, probably but once, of a mild antiseptic is sufficient. We do not recommend nor hold any brief for any one antiseptic. Throughout the country many different skin disinfectants are used in the pre-operative preparation, and an even larger number of antiseptics are applied in the treatment of wounds. There are clinical differences between these antiseptics. And yet the morbidity rates are not widely divergent. Which brings us to the realization that whether an infection will develop or not depends largely on the number of organisms present and their relative virulence, the resistance of the host, and least of all on the antiseptic used."

The common surgical antiseptics are:

Mercurochrome—2 per cent aqueous solution or ointment.

Tincture of iodine—3.5 per cent alcoholic solution.

Hexylresorcinol (S.T. 37)—1 mg. per cc. in 30 per cent glycerin and 70 per cent water.

Dichloramine-T.—0.5 to 10 per cent aqueous solution.

Merthiolate—1:1000 to 1:30,000 aqueous or alcoholic solution.

Metaphen—1 to 2000 in aqueous solution.

Boric acid—saturated solution, 5 per cent.

Methylene blue—gentian violet (MBGV). Methylene blue 5 per cent, gentian violet crystals 5 per cent in 50 per cent commercial grain alcohol.

Alcohol—70 per cent.

Acriflavine—0.05 per cent.

Sterilization by heat and fumigating gases are forms of disinfection but have been considered elsewhere.

The specific sterilization of carriers of pathogenic organisms presents a difficult problem in preventive medicine. Those who are well but harbor typhoid bacilli, meningococci, diphtheria bacilli, and amebic cysts are particularly rich sources from which these organisms are being continually disseminated into the environment. The sterilization of these individuals in respect to their particular pathogens *in vivo* is disinfection applied to specific organisms, or in practice, specific therapy of the "carrier state."

Diphtheria carriers are recognized by routine throat cultures. When found, the organisms recovered should be subjected to the virulence test to determine pathogenicity. Many of these individuals will clear themselves spontaneously in a few weeks. Others remain chronic carriers indefinitely. In the latter group chemical sterilization with the ordinary throat antiseptics such as hydrogen peroxide, potassium permanganate, iodine, hypochlorite solutions, and antiseptic dyes should be tried, but consistently favorable results cannot be expected. It appears that the correction of anatomic and functional faults in the nose and throat offers the best

permanent solution. This consists in the treatment of chronic upper respiratory infections and the correction of such defects as deviation of the nasal septum, hypertrophied turbinates, nasal spurs and the removal of tonsils and adenoids or tonsillar remains from previous incomplete tonsillectomy.

The use of specific immunizing agents such as antitoxin and toxoid appear to have no beneficial effect.

Overplanting of the diphtheria bacillus in the tonsils with cultures of *Staphylococcus pyogenes aureus* has been found to be successful in a few instances.

Meningococcus carriers who have not cleared themselves spontaneously within a month or so after they became carriers from contact with a case of epidemic meningitis or other carriers constitute the greatest problem in the epidemiology of this disease. Unfortunately no certain method is at hand to determine whether they carry virulent or avirulent organisms. The best indication at present is that organisms which are agglutinated by a polyvalent serum at 1 to 100 dilution but are not agglutinated by normal control serum at half this dilution must be held suspect as virulent organisms. The carrier in this case should receive particular attention.

Restoration of the nose and throat of these cases to the best possible condition is the only known effective measure. The use of throat antiseptics, other than steam sprays with chloramine as practiced by the British in the World War, and resort to antimeningococcus serum and vaccines, have produced no satisfactory results.

The general health of the patient should be brought to a high level with adequate diet, sunshine and fresh air.

Typhoid carriers are those who at some time have been infected with typhoid organisms and harbor them in their gall-bladder or some other portion of the biliary tract. Although they usually give a history of clinical typhoid infection a rare instance is found now and then without such history. The great majority of chronic carriers discharge organisms in the stools and may do so constantly or intermittently. Convalescents occasionally show organisms in the urine.

Urinary carriers are best prevented by the use of hexamethylenetetramine during convalescence from typhoid fever.

Disinfection of fecal carriers by chemicals taken by mouth or any other route has not been successful and specific vaccines are without effect. In fact a great majority of carriers already possess considerable agglutinating power in their blood as revealed by the Widal test. This fact is of importance as an aid in the identification of carriers by means of this test.

Most success in sterilization of carriers has been obtained by removal of the gall-bladder. This can hardly be expected to be

completely satisfactory if organisms can be harbored in other parts of the biliary tract as well. Cholecystectomy should only be practiced when typhoid organisms have been recovered by biliary drainage and when no other contraindications to operation, either medical or social, exist.

Until some more effective method is available, the greatest success in the prevention of dissemination of typhoid bacilli by carriers will be the sanitary control of these people, particularly in all matters pertaining to their participation in the preparation and handling of food.

Endameba histolytica carriers may or may not have had clinical dysentery. A considerable number have probably had intermittent symptoms which were attributed to something else and the true condition went unrecognized.

Craig[1] states that it is his opinion that there is no such thing as a healthy carrier and that this term should be eliminated from the nomenclature. This would automatically throw the prevention and cure of the carrier state into the category of the treatment of amæbiasis.

The treatment of the cyst carrier, with or without symptoms, is most safely and efficiently carried out with chiniofon. Three to 4 pills or tablets containing 0.25 gm. (4 grains) each, three times daily for eight to ten days is the course of treatment recommended for an adult. The tendency for this drug to produce diarrhea in the first days of treatment may be obviated by limiting the initial dose to 2 or 3 pills and increase to the full dose if it is well borne.

Many other infective agents, particularly some due to the helminths simulate the carrier state but are in reality only chronic stages of the disease. It is therefore incumbent on the medical practitioner to render all such patients non-infectious as rapidly as possible by thorough-going treatment. Syphilis and tuberculosis, hookworm and ascariasis are outstanding examples of this need. The use of chemicals in their treatment is indirect disinfection and is of more value than all attempts to disinfect the discharges after they have been disseminated into the environment.

[1] Craig, C F Amebiasis and Amebic Dysentery, Baltimore, Charles C Thomas, 1934.

CHAPTER XLV.

SYNOPSIS OF PREVENTION OF PARASITIC AND INFECTIOUS DISEASES.

Actinomycosis.

Actinomyces bovis.
Actinomyces asteroides.
Oral hygiene, prevention and removal of tartar, attention to carious teeth.
Avoidance of grain dusts.
Skin cleanliness.
Possibly by care of actinomycosis in animals and avoidance of contact.
Actinomyces maduræ.
Wearing of shoes and other protection of the feet.
Attention to minor wounds of feet.
Foot cleanliness.

Amœbiasis.

Endameba histolytica
Cure of chronic carrier state of amebiasis cases. Notification.
Adequate treatment of amebic dysentery.
Sanitary disposal of excreta.
Purification of water supplies.
Prohibition of the use of night-soil as fertilizer except activated sludge shown to be harmless.
Thorough cleansing and disinfection of uncooked green vegetables and fruits.
Sanitary examination of food handlers.
Personal habits of cleanliness, particularly as regards contaminated fingers after using the toilet.

Ancylostomiasis.

Ancylostoma duodenale.
Necator americanus.
Protecting foot gear.
Foot cleanliness.
Sanitary excreta disposal.
Treatment of cases.
Ancylostoma braziliensis (creeping eruption)
Bodily cleanliness.
Control of infected dogs and cats
Sanitary care of contaminated soil.

Anthrax.

Bacillus anthracis.
Quarantine and destruction of infected animals.
Sanitary inspection, sterilization and certification of animal products
Precaution in handling infected animals and animal products.
Preventive immune serum in known contacts.
Closure of infected pasture lands.

Ascariasis.

Ascaris lumbricoides.
Cleanliness of hands after contamination with dirt.
Treatment of cases.
Washing and scalding, if necessary, of green vegetables.
Recognition of household infection.
Sanitary excreta disposal.
Turning up and drying of contaminated soil.
Purification of drinking water.

Balantidiasis.

Balantidium coli
Sanitation of pig pens.
Cleanliness on the part of swine handlers.
Thorough cooking of pork meats.

Blastomycosis.

Blastomyces dermatitidis.
Care in handling human lesions.
Sterilization and incineration of contaminated dressings.
Attention to skin wounds, especially those due to wood splinters

Brucellosis (see Undulant Fever).

Cerebrospinal Fever (see Meningitis, Epidemic).

Cestodes (see Tapeworm Diseases).

Chagas' Disease (see Trypanosomiasis).

Chancroid.

Hemophilus ducreyi.
Cleanliness of the genitalia.
Prophylaxis after intercourse—soap and water; medicinal ointment.
Condom.

Charbon (see Anthrax).

Chickenpox.

Varicella virus.
Notification.
Isolation of patient for one week after appearance of eruption and thereafter until crusts have disappeared.
Disinfection of clothes, bedding and fomites of sickroom (concurrent and terminal).
Sanitary precautions by nursing attendants

Cholera.

Vibrio choleræ.
Segregation of cases.
Disinfection of excreta and all objects around or used by the patient.
Nursing precautions
Sanitary excreta disposal.
Purification of water supply.
Cooking all vegetables—disinfection of fruit
Eradication or control of flies and cockroaches.
Prophylactic vaccination.

Clonorchiasis (see Fluke Infections).

Coccidiosis.

Coccidioides immitis.
Disinfection of contaminated dressings.
Personal cleanliness, especially after contact with soil in infected regions (California).

Colon Bacillus Infection.

Escherichia coli.
Skin cleanliness.
Cleanliness after toilet.
Purification of bathing water.
Disinfection of feces-contaminated articles.
Surgical antisepsis and asepsis; operators and instruments; preoperative care of patient.
Control of flies, cockroaches and other vermin.
Disinfection of wounds.
Prevention of constipation.
Specific immunization by vaccines.
Sanitary disposal of feces and urine.
Incineration of contaminated dressings from infected surface lesions.

Common Cold.

Virus of the Common Cold.
Hygiene of the upper respiratory tract; treatment of nose and throat abnormalities and infections.
Oral hygiene.
Prevention of dissemination by sneezing and coughing; use of individual handkerchiefs; sanitary laundering
Avoidance of contacts; individual and *en masse*
("Cold vaccines" are not antivirus. They are directed toward the concurrently infecting organisms.)
Avoidance of chilling, draughts, irritating dusts, gases and vapors.
Ventilation of rooms, homes, public buildings and meeting places.
Ultra-violet light treatment of air.

Crab-louse Infestation (see Phthirius pubis Infection).

Creeping Eruption (see Ancylostomiasis).

Cryptococcosis.

Torula histolytica.
Disinfection of sputum in lung cases.
Dusts?

Dengue.

Dengue Fever Virus.
Segregation of cases within mosquito bars.
Mosquito control measures directed particularly against *Aëdes* and *Culex.*

Dermatophytosis (see Fungus Diseases).

Diphtheria.

Corynebacterium diphtheriæ.

Isolation of cases[1] one week from date of onset and thereafter until 2 successive negative cultures, taken at least twenty-four hours apart, from both nose and throat, have been obtained.

Control of contacts. Children: If immune as shown by a Schick test or on the basis of a previous attack of the disease, may return to school provided they live away from home, or the case is hospitalized, and if 2 consecutive negative nose and throat cultures taken at an interval of not less than twenty-four hours is obtained. Non-immune children shall be quarantined until one week has elapsed from last date of exposure and until 2 negative nose and throat cultures, taken at an interval of not less than twenty-four hours, have been obtained. Adults. No restrictions are placed on adults unless they are school teachers, when they shall be placed under the same restrictions as children. Food handlers and others whose occupation brings them in contact with children have no restrictions if they live away from home. If they live in a family in which a case of diphtheria exists they shall be subject to the same restrictions as children.

Sanitary sick-room regulations

Sterilization of chronic carriers.

Preventive immunization with toxin-antitoxin or toxoid (anatoxin). Antitoxic horse-serum in contact cases

Hygienic habits of coughing, sneezing and spitting.

Diphyllobothriasis (see Tapeworm Infections)

Distomiasis (see Fluke Infections).

Dracunculiasis.

Dracunculus medinensis.

Avoidance of contaminated surface waters.

Cleanliness of skin in infected regions.

Purification of drinking and bathing water.

Treatment of infected cases Disinfection of contaminated dressings, or incineration.

Dysentery, Bacillary.

Shigella dysenteriæ, vars *Flexner*, *Shiga-Kruse*, *Sonne* (Duval).

Sanitary disposal of excreta

Purification of water and milk.

Sterilization or disinfection of raw foods. Thorough cooking of foods.

Control of food handlers.

Personal prophylaxis by cleanliness, particularly of the hands.

Control of flies

Treatment of chronic carriers.

Specific immunization by sensitized vaccine.

Sanitary care and thorough treatment of dysentery cases.

[1] These and subsequent regulations of the Acute Communicable Diseases are from the requirements of the Massachusetts Department of Public Health unless otherwise indicated.

Echinococcosis.

Echinococcus granulosus.

Personal cleanliness, particularly of the hands before eating.

Caution in handling dogs.

Cleansing and disinfection, if necessary, of eating utensils, especially if soiled with dirt.

Encephalitis, Epidemic.

Virus of Epidemic Encephalitis.

Isolation of cases for an arbitrary period of three weeks following the onset.

Disinfection of nose and throat discharges.

Terminal disinfection of sick-room

Endodermophytosis (see Fungus Infections).

Epidermophytosis (see Fungus Infections).

Enterobius Vermicularis Infection (see Oxyuriasis).

Erysipelas.

Streptococcus erysipelatos.

Surgical antisepsis and asepsis.

Disinfection of contaminated dressings.

Hygiene of childbirth and puerperium.

Care of wounds.

Control of expiratory droplets.

Avoidance of contacts.

Personal cleanliness.

Fascioliasis (see Fluke Infections).

Filariasis.

Loa loa.

Protection of the individual from bites of the mango fly (Chrysops).

Fly extermination and control.

Onchocerca volvulus.

Protection of the individual from bites of the buffalo gnat.

(*Simulium damnosum.*)

Gnat extermination and control.

Wuchereria bancrofti.

Protection of the individual from mosquito bites.

Mosquito control measures directed particularly against *Anopheles* and *Culex.*

Fluke Infections.

Clonorchis sinensis.

Thorough cooking of all fish food in endemic areas.

Sanitary sewage disposal.

Disinfection of night-soil.

Fasciola hepatica.

Purification of drinking and cooking water.

Washing and disinfection, if necessary, of all green uncooked vegetable foods in endemic areas.

Thorough cooking of sheep and goat liver.

Fasciolopsis buski.
Washing, scalding or disinfecting water-chestnut and caltrop.
Sanitary night-soil disposal.
Heterophyes heterophyes.
Thorough cooking of fish food in endemic areas, particularly mullet.
Sanitary night-soil disposal.
Opisthorchis felineus.
Opisthorchis viverrini
Thorough cooking of fish food in endemic areas.
Sanitary night-soil disposal.
Paragonimus westermani
Eating only cooked crab and crayfish meat.
Purification of drinking water in endemic areas.
Disinfection of sputum in human lung cases
Sanitary night-soil disposal.
Schistosoma hematobium.
Schistosoma mansoni.
Sanitary excreta disposal
Purification of bathing and drinking water.
Control of snails, drainage, copper sulphate.
Treatment of human cases.
Eradication of the West African Green Monkey (*Cercopithecus sabŏeus*) in Africa and St Kitts.
Schistosoma japonicum
Sanitary night-soil disposal. Prohibition of use of untreated human feces as fertilizer
Drainage canal treatment to combat snails; straightening, cleaning of banks, lime, copper sulphate.
Treatment of human cases.

Food Poisoning (Infectious) (*see Salmonella Infection*).

Foot-and-Mouth Disease.

Virus of Foot-and-Mouth Disease.
Care in handling infected animals and their products
Animal quarantine
Quarantine of animal products
Pasteurization of dairy products
Precautions in human cases; contaminated hands.

Fungus Diseases.

Achorion schonleinii.
Microsporon, spp.
Trichophyton, spp.
Trichosporum giganteum
Use of individual toilet articles
Sanitary regulation of barbers and hairdressers.
Personal cleanliness of hair and scalp.
Individual hats, caps, etc
Avoidance of contacts.
Treatment of cases of ringworm of the scalp and favus.
Endodermophyton, spp
Treatment of cases of tinea imbricata.
Sterilization of clothing, towels, etc.
Avoidance of contacts.

Epidermophyton inguinale.
Personal cleanliness of body, particularly crural regions and feet.
Sterilization of laundry, shoes, etc.
Individual clothing, towels, toilet articles.
Regulation of public bathing places.
Treatment of itch, athlete's foot, eczema marginatum.

Hormodendron, spp.
Treatment of cases of achromia parasitica.
Sanitary laundering.
Individual clothing, towels, etc.

Microsporon furfur.
Treatment of cases of Pityriasis versicolor.
Sterilization of clothing.

Microsporon xanthodes.
Sanitary regulation of barbers and hairdressers.
Treatment of cases of sycosis of the beard.

Microsporum fulvum (mouse)
Microsporum lanosum (dog, bird).
Trichophyton album (animal?)
Trichophyton equinum (horse).
Trichophyton farinulentum (animal?).
Trichophyton felineum (cat, horse, cattle, sheep, dog, pig).
Trichophyton granulosum (horse).
Trichophyton lacticolor (animal?).
Trichophyton mentagrophytes (horse, cow, dog, pig, sheep).
Trichophyton megnini (fowl and pigeon).
Trichophyton ochraceum (animal?).
Trichophyton persicolor (animal?).
Trichophyton radiolatum (animal?).
Care in handling of animals as indicated after each fungus
Personal cleanliness.

Madurella mycetoma.
Care of wounds of the foot.
Cleanliness of the feet.
Shoes.
Disinfection of discharges from lesions of Madura foot (mycetoma).

Gas Bacillus Infection. (see Wound Infection)

German Measles.

Virus of German Measles.
Isolation of patient until one week from the appearance of the rash.

Glanders.

Loefflerella mallei.
Isolation and destruction of infected animals.
Quarantine of animals.
Quarantine, disinfection, certification of animal products.
Disinfection of materials used around infected animals.
Disinfection of discharges, dressings, instruments from human cases.
Caution in handling animals and human cases.

Gonococcal Infection.

Neisseria gonorrheæ.

Venereal prophylaxis:

Chemical; soap and water; urethral instillation of protargol (2 per cent), argyrol (10 per cent); vaginal douche.

Mechanical; condom.

Control of prostitutes.

Premarital health certification and marital health examinations.

Treatment of the case of gonorrhea.

Abstinence from intercourse during the infective stages

Personal cleanliness.

Sanitary disinfection and disposal of contaminated dressings.

Individual treatment of laundry, disinfection of clothing and eating utensils.

Control of infected food handlers.

Credé's method of prophylaxis of ophthalmia neonatorum.

Granuloma Inguinale.

Klebsiella granulomatis (specific cause?).

Personal cleanliness, particularly of the genito-crural regions.

Venereal prophylaxis.

Grain Itch (see Mite Infestations).

Guinea-worm Disease (see Dracunculiasis).

Heterophyes Infection (see Fluke Infections).

Hookworm Disease (see Ancylostomiasis).

Hydatid Disease (see Echinococcosus).

Hydrophobia (see Rabies).

Hymenolepis nana Infection (see Tapeworm Infections).

Influenza.

Hemophilus influenzæ.

Individual precautions during periods of high incidence. Avoidance of crowds, individual handkerchiefs.

Sanitary habits of sneezing and coughing.

Protective masks for attendants

Disinfection of articles contaminated by the sick. Disinfection of nose and throat discharges.

Virtual isolation of the sick.

Segregation of the sick in special institutions, barracks, camps, etc., during epidemics.

Jaundice, Epidemic (see Spirochetosis icterohemorrhagica).

Kala-azar (see Leishmaniasis).

Leishmaniasis.

Leishmania braziliensis (Espundia, Forest yaws).
Treatment of individuals infected.
Protection from sand flies.
Disinfection of discharges from infected cases.
Leishmania donovani (Kala-azar).
Treatment of individuals infected.
Protection from sand flies.
Leishmania tropica (Cutaneous Oriental Sore).
Treatment of individuals infected.
Disinfection of discharges from cutaneous lesions.
Sand-fly control (?).
Prevention of contacts.

Leprosy.

Mycobacterium lepræ.
Notification of cases.
Maritime quarantine; international quarantine.
Transportation regulations.
Segregation of cases in isolation institutions while infective.
Personal cleanliness of those brought in contact with lepers and in leprous areas.
Treatment of the case to render it non-infective.
Parole of lepers.
Disinfection of discharges, contaminated dressings, tissues, etc.
Control of vermin: bedbugs, cockroaches
Sanitary disposal of excreta.

Loa loa Infection (see Filariasis)

Madura Foot (see Actinomycosis and Fungus Diseases)

Malaria.

Plasmodium falciparum.
Plasmodium malariæ.
Plasmodium vivax.
Prevention of mosquito bites.
Mosquito control measures.
Quinine prophylaxis.
Treatment of malaria to render the patient non-infective: quinine, plasmochin, atabrine.

Malta Fever (see Undulant Fever).

Measles.

Virus of Measles.
Isolation of patient until one week from appearance of rash.
Exclusion of nonimmune contacts, children and school teachers, from school for sixteen days from date of last exposure.
Prophylactic convalescent and adult immune serum.
Disinfection of discharges from nose and mouth of measles patients and articles contaminated by them.
Terminal disinfection.

Meningitis, Epidemic Cerebrospinal.

Neisseria intracellularis (meningitidis).

Isolation of patient for two weeks from onset of disease and thereafter until all acute symptoms have subsided.

All children, and school teachers who are contacts, and food handlers who are contacts and living in the family in which there is a case of meningitis, to be quarantined until ten days from date of last exposure.

Sanitary sick-room precautions. Concurrent disinfection.

Determination of carriers by nose and throat cultures.

Sterilization of carriers.

Individual precautions on the part of attendants. Masks.

Mite Infestations.

Glycyphagus domesticus ("Grocer's itch" mite).

Disinfection of food-stuffs.

Disinfection of hay and grasses.

Personal cleanliness.

Leptus autumnalis (harvest mite).

Insect-proof clothing.

Repellents (of little value).

Removal of mite and disinfection of the bite

Pediculoides ventricosis (grain itch mite).

Precautions taken by handlers of grain, cotton, straw Cleanliness; long sleeves; gloves.

Disinfection of straw used for mattresses, etc.

Repellents (of little value)

Rhizoglyphus parasiticus ("coolie-itch" mite)

Protective coverings of arms for workers in tea gardens.

Destruction of mites on vegetation by spraying.

Trombicula akamushi (Kedani Mite).

Clearing of stream banks in regions where Tsutsugamushi fever is endemic.

Rodent control.

Personal cleanliness of workers in the fields and marshes of endemic areas.

Trombicula schüffneri.

Precautions in handling small rodents and birds.

Precautions on the part of workers in tobacco fields

Trombicula deliensis

Precautions on the part of workers on palm oil estates

Rodent control.

Molluscum Contagiosum.

Virus of Molluscum contagiosum.

Prevention of contact with known cases.

Sanitary regulations in public baths.

Moniliasis.

Monilia albicans.

Personal cleanliness, general and genital.

Cleanliness of nipples of nursing mothers.

Sterilization of nursing bottles and nipples.

Cleanliness of mouths of infants

Disinfection of contaminated dressings and clothing in genital and bronchopulmonary moniliasis.

Disinfection with antiseptics of the mouths of patients with thrush

Mumps.

Virus of Epidemic Parotitis.

Isolation of patient until one week of disease and thereafter until all swelling of the salivary glands has disappeared.

Concurrent disinfection of discharges and contaminated articles in the sick-room.

Terminal disinfection.

Mycetoma (see Fungus Diseases).

Myiasis.

Cutaneous, intestinal and *orifice myiasis-producing flies.*

Personal cleanliness.

Dressings on all surface lesions.

Hygiene of nose, ears, eyes and genitalia.

Fly eradication and control measures.

Sanitary regulations of sewage, garbage and excreta disposal, and stable sanitation.

Control of animals with myiasis (Bot flies).

Sanitary disposal of carcasses.

Incineration of dressings, etc., contaminated with organic discharges.

Sanitation of floors of dwellings. Dirt, feces, etc.

Sterilization of food and water contaminated with larvæ of *Eristalis tenax.*

Disinfection of clothing contaminated with organic matter.

Necator Americanus Infection (see Ancylostomiasis).

Onchocerca Volvulus Infection (see Filariasis).

Opisthorchiasis (see Fluke Infections).

Oroya Fever (see Verruga Peruana).

Oxyuriasis.

Enterobius vermicularis.

Personal cleanliness, particularly of anal region.

Washing of hands after using the toilet and before eating, particularly in the case of infected food handlers.

Disinfection of ova-contaminated clothing.

Thorough cooking of food in households with infected members.

Pappataci Fever.

Virus of Pappataci Fever.

Isolation of patient under mosquito bar during duration of illness.

Gnat-proof protection in endemic regions.

Sand-fly control.

Paragonimiasis (see Fluke Infections).

Paratyphoid Fever (see Typhoid Fever).

Pediculosis.

Pediculus humanus, vars. *capitis* and *corporis*.
Treatment of individuals harboring lice.
Disinfection of clothing, bed clothes (delousing).
Avoidance of contacts.
Personal cleanliness.
Sanitary laundry control.

Pertussis (see Whooping Cough).

Phthirius Pubis Infection.

Phthirius pubis (crab-louse).
Treatment of patient harboring crab-lice.
Disinfection of clothing.
Avoidance of contact.
Personal cleanliness.

Pityriasis Versicolor (see Fungus Infections).

Plague.

Pasteurella pestis
Isolation of case.
Prevent fleas from approaching or leaving an active case.
Individual precautions to prevent flea bites.
General contact precautions on the part of attendants.
Use of masks by attendants on pneumonic cases.
Concurrent and terminal disinfection.
Rat and other rodent control measures.
Flea eradication measures
Specific prophylactic immunization by plague vaccine (Strong's vaccine, Haffkine's vaccine).
Maritime and land quarantine.
Disinfection of common carriers.
Sanitary burial or incineration.
Quarantine of all public meeting places.

Pneumococcus Infection.

Diplococcus pneumoniæ.
Prevention of predisposing causes: general low grade of health, exposure, alcoholism, respiratory tract infections, crowding, poor ventilation, street and house dust.
Care in attendance on pneumonia cases: cleanliness, avoid droplet infection; masks. Sterilization of fomites.
Oral hygiene.
Hygienic habits of coughing, sneezing, spitting
Prophylactic immunizing vaccine against Types I and II pneumococci.

Poliomyelitis, Acute Anterior.

Virus of Epidemic Poliomyelitis.
Isolation of case until two weeks from onset of disease and thereafter until acute symptoms have subsided. Isolation preferably in screened room.

Quarantine of all children, school teachers and food handlers living in the family with a case of poliomyelitis for two weeks after the date of last exposure.

Passive immunization of contacts with post-poliomyelitic and normal adult human serum.

Active immunization with monkey passage virus, formalinized virus, and serum-virus mixture is in the experimental stage.

The prophylactic nasal spray of 0.5 per cent each of picric acid and sodium aluminum sulphate in 0.85 per cent saline is on trial with suggestive results. Instillation of zinc sulphate 1 per cent, pontocaine 1 per cent, sodium chloride ½ per cent in distilled water onto the olfactory area of the nose.

Notification by physicians.

Concurrent disinfection in the sick-room.

Terminal disinfection by cleaning.

Avoidance of contact and crowding during periods of high incidence.

Pasteurization or boiling of milk.

Psittacosis.

Virus of Psittacosis.

Quarantine of infected birds or birds from infected regions; particularly parrots, parrakeets and canaries.

Sanitary regulation of pet shops.

Individual precautions in handling and care of susceptible birds kept as pets or used in laboratories.

Disinfection of cages, excreta, feathers, etc.

Precautions in the care of the infected individual; concurrent disinfection of discharges and utensils.

Rabies.

Virus of Rabies.

Licensing all dogs. Impounding of unlicensed strays. Compulsory muzzling. Anti-rabies vaccination of dogs.

Laboratory examination of all dogs which have bitten humans.

Prophylactic vaccination in all persons bitten by rabid or suspiciously rabid animals.

Pasteurization of milk

Precautions in handling infected animals, particularly in respect to saliva. Disinfection of hands.

Quarantine of dogs transported from infected areas.

Concurrent disinfection of hands and contaminated articles in the sick-room.

Notification.

Rat-bite Fever.

Borrelia minus.

Immediate antisepsis of bites caused by rats, mice, guinea-pigs, ferrets and squirrels.

Rodent control.

Individual precautions in handling rodents, particularly laboratory animals.

Concurrent disinfection of discharges from rat-bite fever patients

Relapsing Fever.

Borrelia recurrentis, vars. *duttoni, novyi, carteri, persica.*
Vermin control: bedbugs, body lice, ticks.
Personal cleanliness. Removal of vermin.
Delousing: clothing, bed clothes, premises.
Avoidance of native houses and furniture in endemic regions.
Avoidance of tick-infested ground in endemic regions.

Rheumatic Fever.

Streptococcus, sp.
Virtual segregation of active cases, especially from intimate association with children.
Hygiene of upper respiratory tract. Correction of aëration defects. Tonsillectomy if indicated.
Education: physicians, parents, school teachers.
Periodic health examinations.

Rift Valley Fever.

Virus of Rift Valley Fever.
Quarantine of sheep in endemic areas and in transport to uninfected areas
Inspection of meats in slaughter houses.
Precautions in handling infected animals (sheep) and their tissues and discharges.
Cleanliness of hands.

Ringworm (see Fungus Diseases).

Rocky Mountain Spotted Fever.

Dermacentroxenus rickettsiæ
Tick eradication and control.
Prevention of tick bites.
Prophylactic active immunization with virus from ticks holds promising results for the future.

Rubeola (see Measles).

Salmonella Infection.

Salmonella, spp.
Thorough cooking of meats.
Pasteurization of milk and dairy products.
Purification of water.
Household precautions: refrigeration, cleanliness.
Rodent control (*S. typhi-murium*).
Fly and vermin control.
Concurrent disinfection of discharges and contaminated articles from human cases.
Detection of human carriers and sanitary control of food handlers.
Personal cleanliness.

Scabies.

Sarcoptes scabiei.
Personal cleanliness.
Avoidance of contact.
Prophylactic antisepsis.

Scarlet Fever.

Streptococcus scarlatinæ.

Notification.

Isolation of patient for four weeks from appearance of rash, and thereafter until all complications have subsided and all abnormal discharges from ears, nose, throat, or other body surfaces have ceased.

Adult contacts quarantined for one week from last date of exposure if a school teacher and non-immune.

Non-immune child contacts cannot reënter school unless living away from home one week, and continues to live away from home.

Concurrent disinfection in the sick-room.

Terminal disinfection.

Pasteurization of milk.

Quarantine of infected cattle.

Hygiene of the nose and throat.

Prophylactic immunization by toxin (active), or antitoxin (passive) in contacts.

Schistosomiasis (see Fluke Infections).

Seven-day Fever.

Leptospira hebdomadis.

Rodent control: field mice in endemic areas

Attention to skin wounds, antisepsis, particularly to mouse bite.

Avoidance of contact with water and materials contaminated with *mouse urine.*

Precaution in handling urine and blood of infected humans.

Disinfection of urine.

Sleeping Sickness (see Trypanosomiasis).

Smallpox.

Virus of Smallpox.

Compulsory vaccination of school children. Revaccination of the public during epidemics.

Vaccination of infants.

Revaccination every seven years.

Notification.

Isolation of patient for three weeks from onset of disease and thereafter until all crusts have disappeared and the skin has healed.

All contacts shall be quarantined until three weeks have elapsed from the date of last exposure unless immunized by a previous attack, by a recent successful vaccination, or showing the immunity reaction

Land and sea quarantine especially during high incidence of the disease in districts from which the individuals have come. International regulations.

The use only of immunes for attendance on the sick.

Strict precautions in the sick-room. Cleanliness, protecting gowns and gloves.

Concurrent disinfection.

Terminal disinfection.

Sparganosis (see Tapeworm Infections).

Spirochetosis icterohæmorrhagica.

Leptospira icterohæmorrhagica.

Rat control.
Avoidance of bathing in contaminated water.
Protection of food against contamination by wild rats and mice.
Disinfection of feces and urine of infected cases.
Personal cleanliness.
Prophylactic active immunization by killed culture vaccines have been tried by Noguchi in Japan.

Sporotrichosis.

Sporotrichum, spp.

Disinfection of discharges and contaminated dressings and other articles from infected cases.

Staphylococcal Infections.

Staphylococcus, spp.

Personal cleanliness of skin and mucous membranes.
Hygiene of eye, ear, nose and throat, genitalia.
Surgical antisepsis and asepsis.
Disinfection of discharges and contaminated articles
Treatment of focal infections.
Immediate attention to and care of all wounds.
Pasteurization of milk and dairy products.
Refrigeration of foods.

Streptococcus Infections.

Streptococcus hæmolyticus (var. *pyogenes*).
Streptococcus epidemicus.
Streptococcus viridans

Nose and throat hygiene.
Individual toilet articles
Hygienic habits coughing, spitting, kissing.
Cleanliness of hands.
Sanitary dishwashing and preparation of food.
Control of food handlers.
Refrigeration of food.
Pasteurization of milk and dairy products.
Purification of water
Isolation of infected cows.
Isolation of cases of streptococcic sore throat.
Concurrent disinfection.
Sterile conduct of childbirth and puerperium.
Sterilization or antisepsis of all wounds.
Surgical antisepsis and asepsis.

Strongyloidosis.

Strongyloides stercoralis.

Cleanliness of hands contaminated with earth or feces.
Sanitary disposal of night-soil
Washing and cleansing of raw foods grown in contaminated soil.
Cleanliness of food handlers

Syphilis.

Treponema pallidum.
Thorough treatment of cases.
Notification.
Follow-up of contacts.
Sanitary regulations governing food handlers, barbers, hair dressers, etc.
Premarital health certification.
Periodic health examinations.
Routine Wassermann tests in pregnancy.
Venereal prophylaxis: soap and water; calomel ointment (33 per cent). Condom.
Control of prostitution.
Sex-hygiene education.
Sanitary regulations governing common drinking cups, towels, etc.
Avoidance of contact: kissing, nursing, etc.
Disinfection of discharges and contaminated articles of infected cases.
Abstinence from intercourse during infective stages.

Tabardillo (see Typhus Fever).

Tæniasis (see Tapeworm Infection).

Tapeworm Infection.

Diphyllobothrium latum.
Refraining from eating raw and undercooked fish in endemic areas.
Thorough treatment of human cases.
Sanitary excreta disposal.
Sanitary regulation of fish markets.
Diphyllobothrium mansoni (Sparganosis).
Purification or sterilization of drinking and cooking water in endemic areas.
Abstinence of the use of frogs and vertebrates as healing applications.
Disinfection of discharges from human lesions.
Hymenolepis nana.
Personal cleanliness, particularly on the part of children living in crowded quarters.
Prevention of contamination of food by infected humans.
Rodent control: prevention of access of rats and mice to food.
Sanitary feces disposal.
Tænia saginata (beef tapeworm).
Market inspection of cattle meat.
Thorough cooking of meat.
Sanitary excreta disposal.
Prohibition of cattle from grazing on contaminated pastures.
Thorough treatment of human cases.
Tænia solium.
Market inspection of pork products.
Thorough cooking of pork meats.
Sanitary excreta disposal.
Sanitary care of pigs and pig-pens.
Personal cleanliness of food handlers.
Thorough treatment of human cases.
Sanitary regulations in the preservation of pork products for sale to the public.

Tetanus.

Clostridium tetani.

Immediate antisepsis or surgical care of all wounds, particularly those showing maceration and devitalization of tissues (crushing, cartridge or fire burns); punctures (nails, gunshot, etc.).

Preventive passive immunization with antitoxin if indicated.

Active immunization with tetanus toxoid of those exposed to particular hazards; soldiers, hostlers, farmers, etc., and to those already found hypersensitive to horse serum.

Individual precautions by handlers of stock animals.

Sanitary regulations governing manufacture, inspection and certification of surgical sutures, umbilical tapes, vaccines and other materials made from animal products.

Care of the umbilical cord at birth.

Thrush (see Moniliasis).

Tinea (see Fungus Infections).

Torula Infection (see Cryptococcosis).

Trematodes (see Fluke Infections).

Trench Fever.

Rickettsia quintana.

Delousing.

Personal cleanliness. Care to prevent crushing of body lice.

Prevention of access of body lice to trench fever patients.

Vermin control.

Trichinosis.

Trichinella spiralis.

Consumption of only thoroughly cooked pork meats (one-half hour cooking for each pound of meat). Same applies to wild boar, bear and venison meats.

Sanitary regulation of pork meats for sale. (Cooked or refrigerated at 5° F. for not less than twenty days).

Market inspection of meat is of questionable value.

Rat control, particularly around pig pens.

Only cooked meats and garbage for pig food.

Trichocephaliasis.

Trichocephalus trichiuris.

Treatment of human whip-worm cases.

Sanitary excreta disposal.

Cleansing and disinfection of raw vegetable foods. Sterilization of fruit.

Personal cleanliness, particularly of food handlers.

Trichophytosis (see Fungus Infections).

Trypanosomiasis.

Trypanosoma cruzi (Chagas' disease).
Treatment of infected cases.
Control of the bug, *Panstrongylus megistus*, in its native habitat and prevent access to humans.
Destruction or control measures directed against armadillos, opossums and bats in endemic areas.
Trypanosoma gambiense } African sleeping sickness.
Trypanosoma rhodesiense }
Glossina (tsetse fly) control.
Mosquito bars. Head nets and other protective coverings.
Treatment of infected cases.
Segregation of the infected cases.
Control of animal reservoirs.
Mass movement of populations.

Tsutsugamushi Disease.

Rickettsia nipponica.
Clearing of areas by cutting out and burning before opening for cultivation in endemic regions.
Control of the water rat.
Protective mite-proof clothing.
Antiseptics to mite bites.
Sterilization of clothing and utensils worn and used in the fields.

Tuberculous Infection.

Mycobacterium tuberculosis var. *hominis.*
Notification.
Treatment of open cases to render the sputum bacillus free.
Segregation of infectious cases. Search for contacts.
Removal of infants and children from known active cases. parents, relatives, school teachers, etc.
Hygienic habits of coughing, sneezing, spitting.
Sanitary ordinances against spitting and the use of common drinking cups.
Regulation of food handlers.
Periodic health examinations.
Disinfection of discharges and contaminated articles of active cases.
Pasteurization of milk and dairy products.
General personal hygienic measures: rest, adequate diet, sunshine and fresh air; prevention of fatigue.
Care during pregnancy; intercurrent illness.
B.C.G. vaccine in infancy.
Tuberculin testing and case finding.
Mycobacterium tuberculosis var. *bovis.*
Cattle herd inspection. Tuberculin testing.
Isolation or destruction of infected animals.
Sanitary meat inspection at slaughter houses.
Pasteurization of milk and dairy products.
Cleanliness of cow stables, milking barns, utensils, milkers.
Regulation of food handlers.
Disinfection of discharges and dressings from infected individuals.
Household precautions in preparation of foods, sterilization of dishes.
Sanitary excreta disposal.

Tularemia.

Pasteurella tularensis.

Rodent control.
Tick control measures.
Precautions in handling animal hides, furs, skins and blood.
Notification.
Isolation of infected individuals.
Concurrent disinfection: discharges, contaminated articles.
Prevention of droplet infection.
Cleanliness on part of attendants.
Precautions in handling laboratory animals and cultures.

Typhoid Fever and Paratyphoid Fever.

Eberthella typhi.
Salmonella paratyphi (Paratyphoid A).
Salmonella schottmülleri (Paratyphoid B).

Sanitary excreta disposal.
Detection and regulation of carriers.
Purification of the water supply.
Cleanliness in preparation of food.
Personal cleanliness, particularly in regard to the hands after using the toilet.
Extermination of flies and protection of food from flies.
Sanitary regulation of markets, restaurants, lunch counters, hotels, etc.
Thorough cleansing and disinfection if necessary of uncooked, leafy vegetables.
Certification of food handlers.
Notification.
Isolation of cases of typhoid fever for one week after subsidence of clinical symptoms and thereafter until two successive negative stool and urine cultures, secured at an interval of at least one week, have been obtained, provided that a person who continues to be a carrier may be released under supervision of and after special permission by the Board of Health.
Food handlers living in a family in which a case of typhoid fever exists shall be excluded from their occupation so long as they continue to live in the same house in which the case exists
Concurrent disinfection in the sick-room.
Personal precautions on the part of attendants.
Terminal disinfection.
Active immunization with Typhoid and Paratyphoid A and B vaccines.

Typhus Fever.

Rickettsia prowazeki.

Notification.
Isolation of patient with typhus fever in a room inaccessible to rodents, or beneath netting.
Delousing of individuals, their clothing and environment, when living in crowded unsanitary conditions.
Rat control. Domestic and municipal
Personal cleanliness. Care in brushing fleas and lice off of the body so as not to crush them.
Sanitation of army barracks, refugee camps and the like.
Clearance of fields, cane brakes and plantations of various kinds of underbrush and grasses harboring field mice and other rodents and ticks.
Avoidance of tick bites.

Active immunization by vaccine has been demonstrated to be possible but is at present at a stage of development that does not permit positive statements on its value. A virus-serum mixture is in the experimental stage.

Undulant Fever.

Brucella abortus vars. *bovine* and *porcine*.
Brucella melitensis.

Specific testing of cattle, goats and swine for brucellosis. Elimination of positives.

Pasteurization of cow's and goat's milk and dairy products made from them.

Slaughter house and market inspection for infected hog meat.

Sea and land quarantine of imported animals.

Precautions in handling infected animals and their discharges.

Sanitary regulation of stables, barns and animal compounds.

Personal cleanliness among food handlers brought in contact with herd animals which may be a source of infection.

Notification.

Isolation of the infected patient.

Concurrent disinfection of all discharges and articles coming from contact with the patient.

Quarantine of patients until their urine is free from the specific organisms.

Varicella (see Chickenpox).

Verruga Peruana and Oroya Fever.

Bartonella bacilliformis

Isolation of patient under a mosquito net or in a screened room.

Disinfection of discharges, contaminated dressings, and articles in contact with the patient.

Control of the sand fly and other vermin(?)

Vincent's Angina.

Treponema vincenti (?)
Fusiform bacilli (?)

Oral hygiene and dental hygiene

Personal cleanliness in intimate contacts with infected individuals.

Sanitary regulations regarding common drinking cups and other utensils.

Sanitary regulations governing semi-public and public eating places.

Household hygiene in regard to all utensils likely to be brought to the mouth or contaminated food.

Individual tooth-brush, tooth-picks, etc.

Treatment of infected individuals.

Weil's Disease (see Spirochetosis Icterohæmorrhagica).

Whooping Cough.

Hemophilus pertussis.

Notification.

Isolation of patient for three weeks from beginning of spasmodic cough.

Concurrent disinfection in the sick room.

Non-immune child contacts excluded from school for two weeks from last exposure.

Practical segregation of infants from older children.

Prophylactic immunization by vaccine as soon after exposure as possible or as long before anticipated exposure as practical. An unaltered antigenic extract of *H. pertussis* is in the experimental stage.

Prophylactic human adult immune serum after exposure.

Prevention of droplet infection.

Wound Infection.

Pyogenic Organisms.
Clostridium tetani.
Clostridia of Gas Gangrene

Immediate attention to all external wounds with soap and water and sterile dressings.

Surgical care of wounds and antisepsis if indicated.

Personal prophylaxis by skin cleanliness

Mixed antitoxic prophylactic sera when indicated.

Yaws.

Treponema pertenuis.

Avoidance of contacts with infected individuals, especially child contacts.

Protective dressings. Disinfection of discharges, dressings and contaminated clothing

Early treatment of patients and elimination of surface lesions.

Prevention of contamination of bath water

Individual toilet articles.

Personal cleanliness.

Fly control.

Yellow Fever.

Virus of Yellow Fever.

Aëdes mosquito control.

Jungle mosquito control in regions where jungle yellow fever is endemic.

Quarantine and disinfection of all common carriers coming from infected regions.

Quarantine of individuals not certified safe by port authorities at point of embarkation International regulations.

Notification.

Isolation of patient in mosquito-proof quarters.

Avoidance of mosquito bites by attendants.

Passive prophylaxis by adult human immune serum.

Hindle's prophylactic vaccine is in the trial stage.

CHAPTER XLVI.

CATEGORY VI: PSYCHOBIOLOGIC AND BIOSOCIAL FACTORS AND THEIR EFFECTS.

THE conception of man as a psychosomatic unit implies that the total individual is a continuous organization of structures and functions ranging from those of the lowest physiologic level to the highest mental attributes.

It assumes that there is no material difference between body, mind, a reflex act, a voluntary movement, a physiologic or a psychologic function except insofar as these distinguish different functional manifestations of his total organization but appearing and operating at different levels.

This continuous unity of man can be extended to include his environment so that he becomes a functional part of a greater organization made up of himself, his fellow men and his material environment.

Every part and function of man is dependent on its subsidiary functions and each of these in turn is limited in its operations by functions higher in the scale. This assures internal equilibrium of the body.

In the same way, the individual contributes his part as a function of his social and environmental complex and must live within the restrictions of this greater organization. By so doing he finds himself in equilibrium with the world about him.

But neither his internal organization nor his external relations are static. The body-mind unit is in a perpetual state of flux in which the relationships between its functions are constantly shifting. There is a continuous adjustment and readjustment between functions to meet changing demands. The socio-environmental flux is just as variable and the individual psychosomatic unit in it partakes of all realignments necessitated by the changing conditions.

In the opening section of this work health was defined as a state of relative equilibrium in body form and function which results from its successful dynamic adjustment to forces tending to disturb it. The psychic or mental level of the psychosomatic unit is not exempt from this definition. Moreover, socio-environmental health may be expressed in the same terms. The individual in disequilibrium with his biosocial environment must restore himself or suffer the consequences of social ill-health.

Examination of the disturbances of equilibrium arising in the psychosomatic unit itself, or due to biosocial factors originating

from without will constitute the present categorical approach to the causes of disease.

Man as an adaptive organism, is required to fulfill certain necessary conditions existing between himself and his environment, and between the integrated mechanisms of his growing body. In these external and internal adaptations man satisfies or dissatisfies conditions which appear in the course of his development and growth under the limitations of his genetic endowment. If he lives he must grow to an adult human being; that he does so at all, perfectly or imperfectly as the case may be, depends upon his equipment and the nature of the environmental factors that act upon him. In the course of his growth, and by virtue of his genetic and environmental interactions, he necessarily possesses certain intrinsic needs that must be satisfied; his tissues must be nourished; he must eliminate waste products, he must be able to react to all important internal and external stimuli; he must manifest a relatively well-balanced physiologic mechanism, his intelligence and his ability to remember, form judgments and relate himself satisfactorily to his social environment, must be of a relatively high order. These are real needs, and the satisfaction of them is essential and common to every man. When they are not met the individual departs from the normal in those functions mostly involved and the failure to fulfill the needs is manifested by physiologic, psychologic, and sociologic signs and symptoms of the abnormal.

Since man is a psychosomatic unit, it is postulated that each need of the organism pervades the whole organism whether the need arises primarily from a demand on a low physiologic level or is impressed on it from without as a necessary response to a situation as elevated as a difficult ethical judgment.

Because many of the physiologic functions are carried on in an entirely satisfactory manner without entering the realm of consciousness, attention to them must be left temporarily with the more distinctly physiologic portions of this book. On the other hand all factors will be considered which involve the functions of the organism in its intelligent control over itself, the conscious *response to situations, the coloring of behavior in response to* physiologic needs which require conscious cooperation or can affect the conscious or subconscious self, and every factor which can influence the higher levels of the psychosomatic unit.

The analysis of the psychobiologic and biosocial factors falls readily into three divisions of study: (1) The primary and secondary needs of the human organism which demand satisfaction on the psychobiologic and biosocial levels; (2) the capacities and equipment of the organism with which it can satisfy these needs; (3) the internal and external influences which modify the satisfaction of the needs by favoring, obstructing, inhibiting, or diverting the natural expression of them.

I. THE NECESSARY SATISFACTIONS.

Biology recognizes the existence in animals and man of certain types of behavior that appear to have a strong psychic component but are unexplainable on the basis of acquired reasoning or the use of mental processes which might have resulted from previous experience with the situation concerned. These behaviorisms have been called instincts, a term which explains nothing but implies innate ability of unexplained origin. More recently the attempt has been made to explain some of them at least, as responses to needs which originate in the organism and require satisfaction by the use of mechanisms involving functions on the psychobiologic level. Thus the instinct to satisfy hunger is a response to a need of the whole organism expressed through certain psychobiologic mechanisms that are set in motion to acquire nutrient and satisfy the demands. In the human infant the instinctive ability to suck the breast is a manifestation of such a need—satisfaction complex. If it is unsatisfied the infant shows evidences of dissatisfaction on a level higher than simple physiology. It seems theoretically acceptable to look on some instinctive acts as an attempt to restore physiologic imbalance within the organism in a manner made possible by inborn patterns of behavior.

There are no satisfactory criteria by which behaviorisms can be placed without question in the instinctive category. They reveal themselves on all levels and involve varying degrees of associated psychic manifestations which are confusing in their complexity. The tendency therefore is to reduce the number of instinctive needs to as few as possible and to allow for a number of complex, but apparently basic reactions superimposed upon them. Thus, homemaking is exceedingly complex but may be primarily a need to satisfy a physiologic imbalance in the gonad-soma complex on which has been erected a whole series of behaviorisms determined by experience, learning, precept, and social expediencies.

The most basic physiologic needs arising within the organism which determine the instinctive reactions are those associated with hunger, elimination, lactation, and sex. They all involve functions of the psychobiologic level, invade the provinces of awareness and consciousness, and are subject to higher nervous system control, direction, and modification to meet particular situations in time and place.

These instinctive needs are common denominators of all humans. If it is possible to speak of primary and essential causes within the processes of the psychosomatic unit, these come nearer to being such than any other known factors. Without the need to satisfy physiologic imbalances it is difficult to see how any other activating causes could set the higher functions in motion to attain the end they do. But behind the mechanisms of the instinctive action

tendencies there are further effective causes which bring about the imbalances. The withdrawal of food for example, or the action of some other disease agent may produce prolonged starvation with its accompanying imbalances and the psychic reaction of hunger. The latter then operates as an effective cause to initiate the processes through which the requirements may be satisfied. The instinctive action tendencies are therefore best looked upon as end processes and not like the relatively simple factors which have been considered in the other categories of the causes of disease. In fact, it is largely due to the other categorical factors that the psychobiologic factors are brought into play by disturbance of the mechanisms on which the action tendencies are based.

The superstructures built on the instinctive needs are acquired responses which participate in bringing about the necessary satisfactions. They are, to a great extent, learned reactions in the sense that without experience they would probably not appear with the same complexity and would lose much of their deliberate character. The example of homemaking will again be taken.

This complex act may satisfy the sex and hunger needs but is not essential to either of them. However, in the society in which the individual is found the making of a home in which he can live with his mate and offspring is deliberately undertaken because it satisfies both his basic needs and the habits of the society. In any given society these habit customs are so strong that compliance with them becomes almost automatic. It is in this sense only that they can be called instinctive tendencies. The instinctive needs underlie them but the manner in which they are fulfilled is not essential from the point of view of the individual. But society may lay such high values on the methods of satisfaction that they become accepted as the necessary ways of living and thereby assume the dignity of need-satisfactions which are expected to be carried out "instinctively."

Among these instinctive tendencies Howard and Patry[1] list feeding, shelter, dress and homemaking, play, rest and sleep cycles or rhythms; sex organization and sex tendencies; gregarious and social instincts (the asexual interdependence, attachment and aversions); the defense or attack and submission reactions; vocalization, language, thought or secondary symbolization (imitation, intercommunication).

These reactions and tendencies are no less real to the individual who is aware of them than the underlying instinctive demands of the unconscious. Biologically they are inferior to truly instinctive reactions because they lack the inevitability of the latter. That is, the form in which the instinctive tendencies manifest themselves depend not on their origins but on other determining factors such as

[1] Howard, F. E., and Patry, F. L. Mental Health. New York and London, Harper & Brothers, 1935

training, mimicry, education, social value and emotional bent. They may in fact be so distorted from the original directions of usefulness that they fail to have any determinable survival value for the individual or the race, and may actually become lethal or nearly so.

It can probably be said that true instinct is always right but that the manner in which it is fulfilled will be useful only insofar as the modifying factors satisfy the logic of the instinctive drive.

An important need of the organism is to respond to stimuli through reflex acts. Most reflex acts take place in the unconscious on physiologic levels but many possess associations with the higher cerebral centers so that the reflex process may enter consciousness during some phase of its operation. Furthermore some reflex acts can be consciously controlled to a certain degree.

The nature of the reflex demands that once the stimulus has acted there must be a response. The reflex act is ordinarily vivid and short-lived and if unimpeded, spends its energies rapidly. Whenever some factor interferes with this unimpeded response it inhibits the expenditure of the energies or diverts them into collateral activities, and consciousness of the sensations and physiologic responses that result constitutes emotion. Emotion is therefore more than a reaction to a stimulus; it is a complicated response to the situation in which the stimulus was involved. If the simple physiologic reaction to the stimulus is the only reaction to it no emotions will be aroused.

The reflex acts are primarily protective to the organism and interference with them may be distinctly harmful. The animal frightened by its enemy to the point where it is "glued to the spot" is in a precarious position because emotion has inhibited the natural reaction to run away. In man every shade and degree of emotional reactions occur, some highly valuable and others dangerous to the point of jeopardizing his existence.

All of the foregoing needs have their basic origins in the psychobiologic mechanisms below the level of awareness. Many, if not all, involve degrees of conscious reaction and thereby reveal the participation of the psychic component to some extent. Some possess so much of the psychic aspects that the initiating physiologic mechanisms can hardly be recognized. All possess the common characteristic of being part-functions of the whole organism.

When the psychosomatic unit is taken as a whole it is found that it, like its subordinate functions, possesses a value in relation to its whole existence. This has been so well recognized by all races of man that every culture has resorted to some device to justify man's existence. It has always been considered necessary by man to explain himself; to ascribe some purpose to his existence. Biologically, this idea has been expressed in the principles of evolution; the adaptive necessities of the successful organism; the response of the

living unit to some biologic urge, drive, or cosmic attraction which makes it develop in spite of itself. The human being cannot keep itself from growing and reacting except by self extinction. As a cosmic unit it is therefore responding as a whole to a cosmic need.

In response to the sum total of the biologic needs the normal, average human adult has reached a certain physical-mental-social stature. Growth at all levels has been unimpeded. He has grown within his genetic pattern under the influence of his environment and succeeded in reaching the desired level of his race. The physical proportions of his body, the completeness of his physiologic equipment, the perfection of his higher nervous system and his adaptions to his environment have made it possible for him to attain wholesome maturity.

Behind this perfection lies the fundamental biologic need to reach it as a fair type of his race. The idiot, imbecile and moron, are failure types of serious grade. The psychopathic personalities, psychopaths and delinquents are perversions of the type. The deaf mute, the epileptic, and the physical defective are partial failures of the type on the levels affected.

From the time a new individual is conceived it is faced with the biologic necessity to go on to full maturity. The survival of the race depends on how many succeed in satisfying this need. Consciousness of the need is awakened from time to time and is expressed in thought and action but it is attained mostly by unconscious responses to the lesser necessities arising in the subordinate functions of the unit. Conscious awareness of failure and inferiority, and social feelings and behavior are indications that the organism as a whole can recognize an internal personal need that has been thwarted. Conversely, ambition, success, attainment of desires, and superiority breed satisfaction and the happy feeling that the demands of the personal need have been met.

Concurrent with individual growth and development there appears a complex of necessary participations in society. Man is a social organism and his adaptation to society is as necessary to the full expression of his functions as adaptation to the non-social environment. This too, may be expressed in terms of needs. Without the opportunities for association with his kind, the exchange of ideas and intercommunication, the expression of bi-sexuality and all of the concomitant institutions built upon it, and the restrictions, limitations and privileges imposed on him by the social order, man might develop as a human but it is difficult to believe that he would be a full-functioning specimen of *Homo sapiens*. If it were possible for a human being to be raised with the apes, and the apes alone, and grow to maturity among them he might with good luck reach physical perfection but he could never complete the recapitulation

of his race. He could have no human children and could never know the fulfillment of his social nature.

Man does not live with man simply because he wants to or is forced to do so by man. His social predilections are based on biologic necessities as much as his appetites are founded on physiologic needs. This "living-togetherness" is taken to imply a human need which demands some degree of satisfaction, the more harmonious the better.

In summary, man is a bundle of needs. His physiologic equipment sets up necessary responses to stimuli which create demands upon it. If the demands cannot be met in a satisfactory way the whole organism suffers. Within himself he possesses certain primary necessities characterized by the need to restore equilibrium in some of his functions. In the satisfaction of these needs he is forced to act in ways dictated by the behavior of his race and the almost unconscious manner in which he does so gives rise to the conception that they are instinctive. Although these behaviors result largely from unconscious reactions to whole situations they frequently reveal the participation of the psychic conscious component in them. Above, or probably beneath all of these, is the biologic urge to grow and accomplish. Man cannot ignore this urge if he will other than by self extinction. On the highest level he must conform to his racial obligation to live socially.

On whatever level he may meet with contradictions in the satisfaction of his needs, man gets in trouble. His psychosomatic unit *must* respond, and it is the realm of preventive medicine to make the way smooth for effective complete satisfaction of all basic needs.

II. THE EQUIPMENT AND CAPACITIES.

The *sine qua non* of a satisfactorily functioning psychosomatic unit is a good physiologic mechanism through which it can express its needs. The potentialities for response must be present in the materials intended to express them and the capacities for expression must be of an order to permit the individual to realize at least the average attainments of his race. The ament possesses no more than the basic animal potentialities for simple existence and the imbecile is so lacking in mental capacity as to be educable within very narrow limits. The deaf mute is so handicapped with poor physiologic equipment that it is only under the rarest circumstances that it ever approaches the level of average expression in spite of otherwise adequate inborn potentialities. The individual with physiologic incompetencies of a lesser degree than any of these may compensate for his lack but frequently does not.

Failure of the psychobiologic mechanisms can result from harmful factors operating through the germ plasm or on the developing

zygote. These will be found among the inheritance factors, defects of nutritive elements, the action of poisons, the effects of physical forces and energies, the result of infective parasitic agents and the psychobiologic and biosocial factors. The manner in which these causative factors operate has been extensively reviewed in the preceding sections of this book. The present concern is with their effects on the organism insofar as they interfere with functions necessary for expression on the psychobiologic level.

It has been repeatedly asserted that the entire body acts as an integrated mechanism. This implies that not only the integrating nervous system is involved but every organ, structure and function of the body. However, many defects are so minor or are present in structures whose functions are so remotely removed from overt expressions manifested through the psychobiologic mechanisms that they can be overlooked in this discussion. For example, a simple malformation which produces no feeling of embarrassment or inferiority in its possessor will occasion no abnormal psychobiologic behavior of any importance. On the other hand a hare-lip or club-foot may result in serious mental states in individuals who are socially handicapped or embarrassed by it. It would be impossible to list all of the defects which might influence feelings and behavior, nor would it be a practical list because a single defect might produce psychic reactions under one set of circumstances but not another. In general, any visible defect or one otherwise incapacitating or revealing itself in any way is potentially able to invade the psychic sphere.

Of far greater importance to psychobiology are those alterations of structure or function which directly involve the mechanisms concerned in the need satisfactions; metabolic and assimilative processes; eliminations; sex responses, locomotion and apprehension; endocrine functions; reactivity of the vegetative and sensori-motor nervous systems, special sense apparatuses; the higher intellectual centers. Organic and functional changes in these mechanisms almost invariably show themselves in overt psychic abnormalities.

General metabolic diseases such as diabetes exert special demands on psychobiologic functions. The diabetic is so disarranged in his appetites that he cannot avoid the necessity of reorganizing his régime to meet the imbalances of metabolism. If he conforms to the demands for excess sweets he slips into dietary satisfactions which are diametrically opposed to what he should do. If, on the other hand, he attempts to control his condition under medical supervision he is faced with restrictions which may be almost unbearable. Nervousness and irritability are characteristic of the uncontrolled diabetic.

Primary gastro-intestinal disorders often involve psychic reactions to the altered appetites. The patient either refuses to eat

because of discomfort or has inordinate cravings. He may become so particular in regard to certain foods that the total dietary becomes inadequate and may lead to even more serious imbalances. The choleric dyspeptic typifies the psychic changes characteristic of this group of disorders. The gall-bladder and gastric ulcer cases are outstanding instances of serious interference with the normal demands of body hunger.

There are many disorders of the eliminative processes which present difficulties. Habit is so intimately connected with elimination that any marked change in the riddance mechanisms is likely to disorder the accustomed adaptations. Urgency creates its own problems and sometimes supreme mental effort is required to bring it under control. When it persists over a long period many of the old habits must be given up and this involves serious readjustments which may not always be taken calmly.

Defects of the gonads and sex apparatus reflect themselves on almost every psychobiologic level. The sex functions (considered more widely than simple sex gratification) determine instinctive tendencies to such a degree that any considerable derangement of them will be evidenced somewhere in the total behavior of the organism. The manifestations may be limited to the personality or may seriously disturb the relationship of the individual to his social environment. Without attempting to outline the possible defects of the gonads and their results it is sufficient to recall the wide changes in physical type and psychic behavior of the eunuch and hermaphrodite. Secondary disease of the sex organs and even the secondary sex characteristics are often accompanied by psychic trauma. The first offender with gonococcal urethritis is psychically disturbed out of proportion to the seriousness of the disease and the woman with pelvic disorders of static mechanical nature is manifestly liable to psychic derangement. Bisexual maladjustment due to sex defects is one of the most potent causes of personal unrest and unhappiness and underlies many of the maladjustment problems between marriage partners.

The human organism depends so largely on the ability to move about, grasp objects, and help itself, that any abnormal condition of the motor apparatus places restrictions on the satisfaction of needs through its use.

Limitation in the muscles, bones and joints are embarrassing to the psychobiologic unit which depends on their functioning properly. The lack of responsiveness may prove serious when response is necessary for the safety of the organism. Not to be able to flee from danger or to draw the hand reflexly away from the fire is disconcerting to the threatened individual as a whole. The recently crippled may be so stunned by his restrictions that psychotherapy becomes a more immediate necessity than any other form of treatment.

Coördination of the functions of the human organism is obtained through the integrating endocrine and nervous system mechanisms. These two systems are mutually interacting and are the mediating mechanisms between all other functions of the body.

On the higher levels of the organism action is largely in and through the nervous system but is by no means confined to it. This assures rapid integration of the whole psychosomatic unit from which no part is exempt. Further integration is obtained by means of the internal secretions which are distributed through the circulating media, but in this instance the speed of action and reaction is necessarily only as fast as the regulating substances can be circulated. The combination of nerve and endocrine mechanisms adapts the organism to the necessities for sudden, precipitate reaction to internal and external stimuli and to the relatively slow, deliberate, sustained reactions to needs arising from disturbed internal equilibria.

Although the organism can survive without a completely adequate nervous system and organs of internal secretion, it cannot operate as a normal whole unless these essential equipments are normal. For example, the cretin with a hypofunctioning thyroid need not die, but so long as the function of that gland is abnormal the whole organism is abnormal. In a similar way many defects of the central nervous system are compatable with life but not normal life.

As with the body as a whole there is a hierarchy of functions within the nervous and endocrine systems. Some parts of each are far more indispensable to effective existance than others. Faulty integration between functions leads to malfunction of all parts dependent on this integration, but because the importance of the functions varies the degree of disturbance in other parts must vary. Thus a defect of an important cortical center is likely to produce serious dysfunctions in the whole organism while a change in a peripheral nerve may have little general effect; or failure of the pituitary gland is generally accompanied by profound bodily changes but ovarian dysfunction may produce little more than local physiologic disturbance. Nevertheless it must be re-emphasized that no disturbance at any level can be purely local—the psychobiologic mechanism is always involved as a whole even though the change may not be recognized or demonstrable.

It is assumed that the reader is familiar with the structural and functional arrangements of the nervous system and the organs of internal secretion. Likewise, the wide field of neuropathology and the endocrinopathies are beyond the scope of this work. A few of the important departures from the normal equipment in these systems will be reviewed because of their particular bearing on the functions of the psychobiologic mechanism.

The central nervous system, like all other tissues, is subject to developmental defects. These may result from hereditary faults or the action of environmental factors. Those which primarily affect the nervous system and are listed under inherited defects in this work are: Huntington's chorea, pigmentary degeneration of the retina, hereditary epilepsy, feeblemindedness and insanity, hereditary alcoholism, hereditary hysteria, hereditary criminality, aplasia axialis, multiple sclerosis, hereditary ataxia (Friedreich's), Ménière's disease, deaf-mutism, hereditary glaucoma, paralytic drooping of the eyelid, color blindness, neuritis optica progressiva, hereditary nystagmus, hereditary tremor and liabilities to disturbances of the autonomic nervous system brought about by other precipitating factors. While many of these, particularly hysteria, alcoholism, epilepsy, and criminality, are listed as hereditary it is probable that true inheritance plays but a small part in their actualization and that they are certainly not inherited as such. Nevertheless, these tendencies give some indication that they may be present in the germ plasm and much more must be learned of their mechanisms before they can be deleted from the list. The bearers of such germ plasm defects may be actually lacking in important psychobiologic structures or carry defective mechanisms in them so that the effectiveness with which they can express future needs is often seriously curtailed.

In connection with the subject of inheritance it is frequently claimed that there is true race superiority and inferiority. This is generally referred to race intelligence or educability. Although it may be true that the social complexes of some races of mankind can justifiably be called backward and inferior this is far from saying that this alleged inferiority is due to lack of natural intelligence. There is no real evidence that any races of *Homo sapiens* are relatively lacking in their intellectual capacities. Mental inferiority appears in individuals in civilized as well as backward races.

The vegetative or autonomic nervous system is peculiarly exempt from the lists of actual physical defects occurring in the nervous system. This may be because it represents the earliest functioning portion of the nervous system phylogenetically and is therefore relatively less liable to change than the more specialized higher nervous system functions, or that an embryo with a demonstrably defective vegetative system cannot live. Whatever inherited defects it does reveal appear to be of the nature of functional disturbance in the direction of increased or decreased sensitivity. With such a defect as a possibility it is believed that the organisms will over- or under-respond to stimuli involving the autonomic nervous system.

Acquired defects of the sensori-motor nervous system result from any of the other possible agents of disease. Nutritional defects are capable of restricting psychobiologic activities to extreme degrees.

Intoxicants and poisons can bring about profound changes that absolutely prohibit continued existence or so alter the nervous system reactivity that the individual can no longer express even the most primary needs of the organism. Physical traumatism, heat and cold, electricity, ultra-violet, *x*-ray and other electromagnetic forces, barometric pressure, and climatologic factors can all affect the nervous system detrimentally. The response of the body to invading organisms is mediated to a considerable degree by the nervous system. These agents may also invade nerve tissues directly and produce irremediable damage. In each instance structural or functional changes may be brought about which will be manifested in nervous system signs and symptoms, frequently of serious magnitude.

The glands of internal secretion occupy a high position in the body economy. These isolated groups of cells have reached such a high degree of specialization for the satisfaction of needs in other cells and tissues that any failure on their part means the withdrawal from the body of some of its most necessary substances.

Unless there is a hereditary lack of the development of the endocrine tissues, disturbances in their mechanisms can result only from effective causes operating upon them. The importance of this conception lies in its contradiction of the impression that the glands of internal secretion, particularly the pituitary, enjoy an autonomy denied other tissues. They are frequently referred to as the "masters" of the body with the harmful connotation that they originate the changes in themselves and are superior dictators of all of the bodily activities. On the contrary, the endocrines are the master servants of the body and respond to innumerable commands given them from the external and internal environments and from each other. No endocrine organ over- or underfunctions without due cause. Their total functions are end-processes and they are not themselves primarily causal. For this reason these organ secretions cannot alone constitute a category of the causes of disease.

The organs of internal secretion are subject to all causative factors which can affect any other tissues. They can be hereditarily poor in physical equipment and can be adversely affected by nutri-*tional defects, poisons, traumatisms, infections and influences* operating through the nervous system. As shall be shown later a normally responsive set of glands of internal secretion is essential for normal operation of the psychosomatic unit, and for this reason good equipment in these structures is necessary for the normal satisfaction of the needs and satisfactions now under consideration.

In summary, a normal physiologic equipment on all levels of organization, is a *sine qua non* of normal psychosomatic activity. The organism may exist as a whole and operate as a whole in spite

of inadequacies in its equipment and capacities, but it falls short of its mark just to that extent to which the inadequacy is important or unimportant to the needs of the whole organism. When the equipment defect involves functions on the psychic level overt evidences of abnormal activity and response in the psychobiologic mechanisms are likely to be present; the imbecile, cretin, deaf-mute, paretic and alcoholic are typical instances of abnormal psychosomatic units whose defectiveness is due in greatest part to an equipment that can no longer respond properly to psychobiologic demands.

III. MODIFYING INFLUENCES.

The normally developing embryo has its needs satisfied immediately as they arise. The reflex and integrating mechanisms develop coincidentally with increasing demands of the organism as it grows in complexity and specialization of its parts. Most of the stimuli are somatic in origin or brought to it by the maternal blood and *therefore operate through the internal chemical and nerve ceptors* developed to respond to them. It is also affected by immediate tactile stimuli to its surface and the response to these is prompt and proportionate to their urgency. In general terms, the embryo or fetus is said to be a purely adaptive mechanism. Whenever disequilibria arise readjustments satisfy them in a direct manner that does not call into play the many indirections of action that characterize the post-natal period. So long as the environment is not too hostile to the embryo it is in a state of perfect adaptation.

Immediately after birth, when the human organism for the first time becomes independent insofar as physiologic capacities is concerned, it becomes dependent for the satisfaction of many of its needs. From the very beginning of postnatal life the human infant *becomes dependent on society. It can grasp the mother's breast* only if the mother brings the breast in contact with the tactile receptors of the infant's hands or lips. When it is deprived of nourishment too long it expresses its needs visibly and audibly; it becomes restless and cries. Under normal circumstances a physiologic disequilibrium is aroused in the mother by virtue of a need to eliminate milk and restore the imbalance of her entire organization. On this instinctive need and her whole sex organization the mother has created a complex set of feelings and obligations toward her infant which makes her act toward it in an "instinctive" way which, when carried out satisfies both herself and her infant.

It is probable that after it has once been placed to the breast the infant will never again react in the same way as at this first experience of dependent satisfaction. At this experience the infant uses new tactile channels which become useful for the acquisition of nourishment, and at the same time experiences stimuli which

primarily have nothing to do with acquiring food. It is petted and bedded in such a way that the new sensations accompanying these acts become associated with the mechanisms of getting something to eat. Although it may be difficult to prove that definite conditioned reflexes arise out of these associations the situations which are created and the responses to them give all the appearance of conditioning.

Thus from the very beginning of postnatal life the human being becomes a complicated reacting organism. It is aware and conscious of its existence and its environment. The primitive needs still exist and demand satisfaction, and given an adequate functioning psychosomatic organization, the needs *will* be satisfied—but they will be modified, sometimes to a very slight extent, but often to a degree that makes them almost unrecognizable. All of the influences which are effective in modifying the innate reaction patterns of the newly-born constitute the subject matter of the present discussion.

The study of human behavior can be undertaken from the physiologic, psychologic or philosophic points of view. Because no one of these approaches can be exclusive of the others it is necessary to view man as a physiologic mechanism which reacts in a particular way to its environment (physiology), and reveals at least a part of this through its psychobiologic organization (psychology), and in so doing satisfies the logic of the universe by actualizing in part the ideas and universals which exist independently of all humans (philosophy). Put in another way it means that physiologically man is material and his physiologic functions are expressions of the relations between material aggregates set up to carry out these functions; that his psyche is his whole organization which relates the psychosomatic unit to everything other than itself; that beyond the psyche and the environment are logical truths and laws to which he is subject because they are atemporal, non-particularized realities that supersede his actualized material, action, thought and reason. The attitudes of the physiologist, psychologist and philosopher are well shown in quotations from the published writings of three contributors to the knowledge of human behavior. Out of fairness to them it must not be implied that the selected quotations represent the whole or even main approach to their thoughts on man but clearly express their thinking on the several aspects of man's personality. Crile summarizes his work, "Man—An Adaptive Mechanism,"[1] with the following: "In the texture and form of his bones and joints; in the structure and distribution of his muscles; in the covering skin and the padding fat, in the nature and distribution of his nails and hair; in the structure and equipment of the mouth, the stomach and the intestines, of the kidneys, ureter and bladder and of the organs for

[1] Crile, G W Man—An Adaptive Mechanism, New York, Macmillan Company, 1916.

procreation and respiration; in the distribution of pain ceptors, and of the defense mechanisms against dust, debris and insects, against cold and heat, and against infection and bleeding; in the mechanisms for appreciating sound and light, color and form; in the mechanisms for taste and for smell, for maintaining an even body temperature, for producing muscular action and for expressing the emotions; in the nature and incidence of laughter and weeping; in the chemical defense against bacterial invasion and against the poisons of pregnancy and auto-intoxication; in the mechanisms of conception, of pregnancy and of birth; in the fabrication of thought; in the mechanisms of communication by natural, spoken and written language; in health and in disease—in the complete life cycle of the *individual from conception to death we see clearly here and dimly* there the mechanisms by means of which a sensitive being immersed in a hostile environment effects survival, we see man—an adaptive mechanism."

Devine,[1] in support of psychology says, "We have felt it desirable to refer to the distinctive features of vital activity at the unconscious physiological level, because there is a tendency to think of physio*logic behavior under one head, and 'mental' behavior under another.* The line of demarcation is not between physiological and mental, but between living and non-living; and the distinction we are apt to draw between physiological activity and overtly manifested conduct is quite unjustified." And further on, "Activity at the level of consciousness must be considered as a modality or special aspect of vital activity. Except for methodological purposes, thought and consciousness cannot be considered independently of the organism, any more than cellular activity can be considered apart from protoplasm. Psychology concerns itself with additional facts about the organism which are ignored by physiology. Physiology deals with the organic functions and activities which are necessary for the maintenance of life, and psychology with the functions and activities concerned with the adjustment of the individual as a whole to his surroundings. In a word, it may be said that the organism with which the psychologist deals is not merely a physical organism, it is a biopsychic organism."

Friend and Feibleman,[2] as philosophers, have this to say, "When the particular function which is the human being becomes actual, it is expressed through the variable subsidiary functions. Viewed, then, in the historical order the human function requires time for its expression. Thus to rise to consciousness, there must be more than instantaneous awareness, *i.e.*, an awareness of invarient relations in

[1] Devine, H.: Recent Advances in Psychiatry, Philadelphia, P. Blakiston's Son & Co., 1933.

[2] Friend, J. W., and Feibleman, J. K.: The Unlimited Community, London, Allen Unwin, Ltd., 1936.

terms of which change is made intelligible. This 'memory' is another way of saying 'consciousness.' This explanation will perhaps be made clearer by recalling that the whole human organization is a series of functions which persist more or less, few of which rise to consciousness. The beating of the heart and what are called acquired habits, unlearned and learned reflexes, etc., can be viewed metaphorically as unconscious memory, in order to show that memory is consciousness of functions.

"Enough has been said to indicate what the realistic orientation toward psychology must be. It must work from the independently known world back to the mind which apprehends it, even though this seems to be a reverse process. For the other approach is an impossibility since nothing whatever can be known, as we have shown, except in terms of universals. Thus the order of learning must be reversed in order to understand even the order of learning."

Necessity for a unitarian point of view is seen when it is realized that the factors which influence and modify psychosomatic activity are as diverse as reflex stimuli, fear, and abstract thought.

As the human being is observed from infancy, through childhood and adolescence, to the adult state the impression is gained that there has been mental as well as physical growth. From the simple reacting state of the infant to the complicated mental activity of the adult there has been an increase in the types and forms of reaction patterns, a multiplication of associations between past and present events, and an increasing ability to exercise judgment, to utilize reason and to abstract. Growth and development are terms borrowed from biology and may be retained in their application to mental processes if not taken too literally. Too little is known of the processes of increasing mental complexity to be positive that "mind" grows in the strictly biologic sense.

Complexity in behavior, thought, and action results from the summation of impressions on a psychobiologic mechanism which is genetically prepared to receive them. This takes place in the historical order and the organism once having received these impressions reacts to them thereafter in a more or less orderly manner according to their kind and intensity. It appears to be immaterial whether the responses to these impressions rise to the level of awareness or remain in the unconscious life of the individual. The point of greatest importance is that mental complexity evolves under a continuous series of influences which operate in a more or less haphazard manner over a period of time. Theoretically, if all individuals received entirely similar impressions at exactly the same chronological ages it is questionable if there would be much difference between their personality types. A shadow of such a possibility is seen in the superficial similarities in the thoughts and behaviors of people living together under the same cultural influences. All

Hottentots behave more like Hottentots than metropolitan Westerners. There are individual differences between Hottentots but they all possess a common denominator of behavior which results from their being raised in a Hottentot culture.

All humans possess a common mode of behavior independent of the culture or society in which they are raised. This fundamental basic human behavior may be likened to the human genetic pattern and in all probability is a part of it. On it is built the superstructure of the individual personality which is the basic pattern altered and extended by a wide series of physiologic, psychologic, and social influences that affect it without cessation all through life.

Gesell[1] has adequately described the basic responses of the developing infant. This author has selected certain important behavior items which he believes may serve as "normal indices of mental growth." The items selected are not arbitrary, but were arrived at by prolonged observation of many infants under experimental conditions; the indices are according to Gesell, normal basic tendencies of normal infants at particular chronologic ages. To quote, "Because development follows sequence and tends to keep to an established tempo, it is possible to regard certain characteristic forms of behavior as indices of mental growth. Such indices do not have the absolute accuracy of inches and pounds, but they have a symptomatic value in relation to age which makes them indispensable for defining an estimate of developmental status. At birth the infant clasps reflexively a cube pressed into the palm. At one month he looks at the face of a person standing near his crib. At two months his eyes follow a person moving near his crib. At three months he holds and manipulates a rattle. At four months he closes in on a ring which is dangled above his chest. At five months, when held at a table in a sitting position, he grasps a cube on contact. At six months he reaches for and grasps the same cube on sight. At seven months he looks for a fallen spoon. At nine months he brings a spoon into combination with a cup. At ten months he can pick up the above-mentioned pellet with precise pincer-wise prehension. At eleven months he pokes a rod into a hole. At twelve months he may say two 'words.' "

If these criteria are generally true it means that the infant in passing through this formative period reveals increasing complexity in its response to tactile and distance stimuli, and in neuromuscular coördination, conditioned reflexes, memory, thought associations, and the use of symbols. At the termination of the first year it shows some capacity for judging and reasoning.

The only danger in setting down Gesell's criteria in the above form is that it appears to oversimplify the problem. Actually each

[1] Gesell, A., in Practice of Pediatrics, Hagerstown, W F Prior Company, vol 1, 1936.

criterion is a highly complicated affair. The fixation of attention on an attendant passing the crib is far more than the simple eye and head movement which is observed. It is a highly conditioned reaction of the infant organization to the total situation. For two months attendants have been passing the crib and the infant's retina has been recording the fact. It is impossible to know what other associations have been going on in the infant brain and what distant changes have taken place in other parts of this psychosomatic unit. That they have been widespread and important to the developing personality cannot be doubted when consideration is given to the intricacies of coördination and integration necessary to follow an object *deliberately* by turning the head and eyes. At the stage where the infant reaches through space to grasp the teething ring suspended before it, many complex associations and responses must be necessary to make the baby *go to* an object with which it is not even in contact.

In spite of all wonder at the phenomenon, all normal infants go through a similar progressive development peculiarly correlated with chronologic age. Insofar as they do so they are revealing the basic criteria of development. But to the observer, trained or untrained, these critical acts are enveloped in a maze of less tangible activities that set one infant apart from all others. There are all degrees of responsiveness, hesitations, decisions, and inhibitions in the performance of the acts. *Overt personality* thus begins to show itself early. It has been well described and defined but it has defied explanation. Undoubtedly it is largely due to conditioned reflexes which have been built up on the primary need responses. Although these may give the impression of instinctive reactions, no real necessity can be found underlying such possibilities as the ability to poke a rod into a hole. No adequate motive is forthcoming to explain such phenomena; the assumption that these acts may have adaptive or survival value is too normative for scientific use.

And yet each infant is an individual and expresses its own individuality. In each baby the course of development is basically the same but the total result is different. It appears that this can be accounted for only by assuming that the same fingers have played the same notes on equally responsive instruments but in different keys and tempo. The total situations with which each infant is faced day after day have fundamentally the same components but differently arranged and timed.

In all the foregoing no attention has been paid to the problem of how repetition or temporal spacing of events in the past can affect the present. The question has not heretofore arisen "How can an experience at one moment have any influence on a similar or almost similar one minutes, hours, or days later?" The answer is ordinarily given by resorting to explanations in terms of memory, action

patterns, or "final common pathways" of conflicting stimulus reactions. To aid the first, engrams are postulated as lasting impressions on the plastic nervous tissue; action patterns are bolstered by the conception of fixed associations between nerve elements, which once established become permanent; the final common pathway implies that repetition of impulses diminishes the resistance of the pathway over which they travel so that the threshold is lowered for future stimuli which will then travel over it in preference to others.

Memory is the *sine qua non* of consciousness and the two may be taken as different ways of saying the same thing (Friend and Feibleman), because the human being (as a function) requires time for its expression, *i. e.*, a succession of events in the historical order, and this results in awareness of change. In other words, a single experience which is instantaneous could not give rise to consciousness because there would be no awareness of change; on the other hand change could not be recognized unless there was a relationship between successive events, *i.e.*, consciousness of change, or memory.

For psychobiology, memory is accepted as a real datum of experience but its mechanisms remain unknown. It appears that past experiences are remembered on all levels of the organism. Rignano believes that such physiologic processes as assimilation, cell specialization, etc., are all possible only on a mnemonic basis. All psychologies recognize the influence of the past in the present. To those may now be added the philosophic conception that memory of the past is essential for consciousness in the present.

The problem of the development of individual personality can be reduced to the relations between two variables; an integrated remembering organism which by some unknown process is able to project its past experiences into its present activities and a changing environment which is able to affect the organism through sensitive receptor mechanisms that can react to it. Change is the important function on each side of the equation.

The developing infant is a changing infant submerged in a changing environment. The historic nature of the changes and the fortuitous occurrence of experiences with the environment makes it sure that no two infants will have entirely similar histories. And because the environment may or may not always satisfy the elementary needs of the organism as they arise, the infant is subjected to what it probably looks upon as a friendly or an unfriendly world. It is probable that adaptation of the infant to its environment is seriously stressed many times, but it is also probable that it undergoes more experiences where the environment is favorable to it. Progressive development seems to be possible only when tensions exist, for a state of perfect equilibrium would be found only in death.

Out of this apparent chaos comes order, recognized as normal growth and development with, it must be understood, scars and wounds of failures and frustrations which have a peculiar liability to persist. The scars, however, serve a useful purpose, and appear to be the basis on which the psychically active organism builds its values. By having been thwarted in many of its satisfactions the infant has been faced with contradictions and has attained its ends by resorting to a primitive selection, not necessarily reasoned, but gotten by finding out on repeated occasions that success followed certain alternatives of behavior.

Observations on the infant indicate that at this early age it has developed all of the type reactions that characterize the human personality. It has experienced all of the fundamental needs of the organism; it has reacted to pleasure and pain; it has had reflexes conditioned by associated stimuli; it has shown particular reactivity toward the mother or her substitute; it has expressed many of the primary emotions; it is aware of itself, its material environment and people; it has likes and dislikes and expresses satisfaction and dissatisfaction; it has attempted communication; it has learned by repetition of experiences; it has developed aggressive tendencies and docility. There can be little doubt that these are real objective data, and not subjective inferences on the part of the adult observer.

Of great importance is the fact that these reactions are not equally developed in all infants. Although Gesell has shown that they develop chronologically there are wide variations in the amounts of the behavior criteria in different infants at similar ages. This implies that some infants may be more aggressive than others, more emotional, more conditioned, etc., at the same chronologic age.

It might be justifiable to liken the infant to a "personality embryo" and look upon these earliest buddings of the personality components as *anlage* of future personality functions. There is no implication in this that the personality has become fixed. On the contrary it remains plastic for years to come. What characteristics become modified and changed to a radical degree or persist as they are through life, depends on the order, intensity, and importance of the elements in future experiences. (Some would make allowances for hereditary tendencies in personality types but it seems unnecessary other than to admit that hereditary defects may be present in the biopsychic equipment and so limit the ability to express certain personality components.)

Before considering the factors which modify behavior to the detriment of the organism it is necessary to amplify the total phenomenon of reaction to a situation as a whole. This does not imply that the organism reacts to a whole situation; there may be

elements in the situation of which it never becomes aware, and many reactions seem to indicate that it reacts to elements which are not even in the external situation. The truth seems to be that both assumptions are correct. Reaction is just what the word implies, a relation between the affector and the receptor; an interplay in which both take part. But it has been shown that the receptive organism is in flux and through memory can reënact experiences of the past. If then the present response is participated in by an organism which can project the past into the present, it is not remarkable that present reactions do not seem to conform to expectations drawn from the nature of the situation. It appears to be immaterial whether the memory component of the reaction remained in the unconscious or invaded consciousness. The unpredictability of situational reactions is at the bottom of all attempts to understand the significance of the psychobiologic and biosocial influences which modify behavior.

From the foregoing discussions it is apparent that causality in abnormal psychic states cannot be reduced to single causes. What might appear to be an effective cause in one situation may be inadequate in another, in spite of the fact that in one the intensity of the factor may be greater than in the other. It is plain from studies in psychiatry that influences which produce abnormal psychic states may be the same as those which are responsible for normal behavior and that in the absence of other adequate causes much of the difference lies in the relation that the situational factors bear at the moment to the state of the receptive organism at the same moment.

Repetition is one of the necessary qualities of reactions which have any considerable tendency to become fixed. It is seen in the development of conditioned and learned reflexes; it appears in the development of habit; it is a fundamental requirement in learning. Similarly, it is present in the acquirement of harmful attachments, thought associations, attitudes of superiority and inferiority, obsessions, habituations, and many opinions, prejudices, and similar biased mental attitudes.

The individual who experiences a psychic event receives an impression of the total reaction as some pattern of conscious or unconscious mental activity. This mental response may or may not be revealed to an outside observer. Even if it remains entirely within the unconscious the subject may subconsciously show objective signs of the reaction by overt behavior. If the subject becomes aware of the psychic event he may deliberately direct his response so that it becomes evident to an observer, or he may inhibit his reactions so that he alone knows the content of his experience. In each instance the psychic pattern of the event is present as a reality whether it be revealed subjectively or objectively. From this contention an im-

portant postulate is derived: that in every psychic event, mental experience, or behavior response to a situation, there arises a dominating impression that is the resultant of the subjective elements in the mind at the moment and the objective components of the situation. It might be likened to a chord struck on an instrument which blends with another chord sounded simultaneously on a second instrument. The result will be either harmony or discord, but which ever it may be it will dominate all of the elements from the two chords which went to make it up. A more definite psychic example may be cited in a person who is concentrating on some problem in ethics and whose mind is full of the subject matter pertaining to it. If now, while the mind is in this state, a related ethical question is suddenly presented to him it is highly probable that he will have a clear understanding of the implications in the question. Had he not been so absorbed in thought on similar subject material at the moment it is questionable that he would have had such an accurate reaction and may even have been seriously upset by the question. Here it is seen that the psychic reaction is dominated by the mental pattern that resulted and assumed control.

It should be possible therefore to determine the objective and subjective elements in any situation, which when brought into combination, will result in more or less predictable mental dominations which direct behavior. These would constitute the real modifying influences of behavior and become objective data of experience.

1. **Feeling or Affection.—Pleasure.**—Pleasure, according to Russell[1] "is a property of a sensation or *other mental occurrences* (italics author's), consisting in the fact that the occurrence in question either does not stimulate any voluntary or reflex movement, or, if it does, stimulates only such as tend to prolong the occurrence in question."

Pleasure is not an inherent quality in a sensation or mental occurrence but emerges only when the components of the object-mind relationship are such as to be able to elicit it. Pleasant stimuli may under other circumstances become painful to the psyche. One may experience an enjoyable sensation in the performance of a love act under one set of conditions and be overcome with revulsion by the same act under other conditions. The stage must be set for pleasure, otherwise there will be no pleasure.

Pleasure arises out of innumerable mental events. It is evident most elementarily in the satisfaction of the primary body needs; the instinctive restoration of equilibrium. It pervades the sense of superiority and the successful accomplishment of tasks, it dominates self-sacrifice, ambition, social acceptance, and helpfulness.

If pleasure is experienced, consciously or unconsciously, it dominates all other elements of the situation which aroused it and

[1] Russell: The Analysis of Mind, New York, The Macmillan Company, 1921.

modifies the immediate behavior response in such a way as to take the best advantage of it.

Discomfort.—Discomfort to Russell, "is a property of a sensation or other mental occurrence, consisting in the fact that the occurrence in question stimulates voluntary or reflex movements tending to produce some more or less definite change involving the cessation of the occurrence."

All that has been said about pleasure can be stated about discomfort. It is equally as dominant when it is aroused and it too requires that the stage be set. Painful self-sacrifice can be turned to pleasure when the other elements of the situation accord more with pleasantness than discomfort. Discomfort is the dominating element in failure, revulsive feelings, useless (to the individual) sacrifice and self-denial, thwarted ambition, feeling of inferiority, persecution and blame, repressions and general maladjustment.

2. **Emotion.**—When feeling has been aroused through the contents of a psychic event and the simple primary response to it is inhibited or diverted, emotion emerges and takes over the situation. It is importunate and dominating until at least some of the energies which it mobilized have been dissipated in action.

Emotional response is not inherent in the stimuli of an event but appears only when the stimuli strike a sympathetic chord in the mental state of the subject at that moment. If one is prepared for danger and on the alert no emotional response need result when the danger actually appears. A threat to be struck may be accepted calmly if the mental state at the moment is not sensitive to threats. Emotion is inevitable only under given circumstances, but when it appears it dominates immediate subsequent behavior.

Under certain circumstances the emotional reaction may be so intense as to result in physiologic shock. When the feeling and action relation is diluted by time and associated with successions of unpleasant mental events the resulting emotion appears more as stress than shock. This manifests itself in anxiety, worry, apprehensiveness, irritability, over-sympathy, sentimentality, over-enthusiasm, fanaticism and the psychic reactions of anger, grief, silliness, and untoward expressions of affection. The kind and degree of emotional response is therefore determined not by a mechanical inhibition of feeling but by the nature of the elements in the event that modified the significance of the feeling which was aroused.

3. **Ideas.**—Ideas become actualized in the mind through self-synthesis or by the presentation of symbols from without. Gesell's infant who reaches for a teething ring must apprehend a relation*ship existing between itself and the ring in space. The relation* was always there but the infant was unaware of it other than as a simple visual impression of the ring. When the action patterns enabled it

to reach for the ring it became aware of the space relationship and apprehended the idea.

When the growing child repeatedly sees a picture of a horse it sees just that and nothing more. But when mother keeps repeating "horse" with the presentation of the picture the child eventually apprehends the relationship between the two kinds of symbols for the universal horse.

The schoolboy suddenly understands that multiplying is just another way of adding and thereafter makes use of this new idea (to him). The development of appreciation and understanding of the relations existing between notes of the scale, colors, cause and effect in physical relationships, economic principles, scientific deductions, are all examples of apprehended ideas. Actualized ideas multiply at a rapid rate all through the years of learning and the presentation of the proper and logical relationships between them is the method of education. This does not imply that all apprehended ideas are properly understood, or that they must necessarily be true. But in either event the ideas become real to the possessor.

It was stated earlier in this section that memory was the consciousness of relationships between events. It now becomes evident that memory is also consciousness of the relationships between ideas for ideas are real events even if the subject is the only one aware of them. Thus, whenever one is aware, he is aware not only of external events but of internal memory events (thoughts) also. Ideas swarm through consciousness and are always present when the elements of external situations are presented to the mind. This results in a comingling of memory events and the impressions from the present situation. The mental pattern resulting from this merger appears to determine to a great extent the subsequent behavior of the individual. This apparently simple principle is complicated by the intrusion of unconscious memory into the patterns; ideas of which the individual may not be consciously aware.

It is hardly necessary to emphasize the importance of existing ideas and thoughts of the moment on the direction of subsequent behavior. If ethical ideas are present in one individual and not in another the response to an ethical situation will not be the same in each. The reaction to a set of empirical data will not be the same to a non-scientifically trained person as to a scientist.

As important as ideas are to the determination of human behavior they are only so to the extent that they dominate feelings and emotion in any given situation. Thus ethical judgment may be entirely overshadowed by an intense emotional component and a worthy idea may not be acted upon if to do so is painful.

It is within the most frequently repeated combinations of ideas, affective states and emotional responses in the individual's psychic life that explanation will be found for his personality make-up and

behavior. These three psychic elements in every psychic event have the power through permutations and combinations to modify behavior under any situation into an innumerable variety of patterns. But because the human infant in a given group culture passes through experiences very much in common with every other infant in that group and grows to adulthood with fixed cultural ideas of the group it is not surprising to find most members of the group thinking and acting much alike. Individuals stand out here and there who differ from the herd. They do so either because of some hereditary or acquired defect in their psychobiologic equipment; on account of deep-seated alterations in their physiologic state (puberty, pregnancy, gland therapy) or because the consequences of the clash between their mental experiences and the demands of their environment have departed from the average, *i.e.*, their personal history differs in important particulars from the common history of the group. When they depart too widely they are looked upon as queer, geniuses, or insane.

CHAPTER XLVII.

THE INFLUENCE OF PSYCHIC FACTORS ON PHYSIOLOGIC FUNCTIONS.

It is recognized that every reflex stimulus which enters consciousness carries an import of pleasure or discomfort and that if either of these elementary feelings is inhibited and the normal response to them is interfered with it gives rise to emotion. The emotional response is mediated through the thalamus and the vegetative nervous system centers in the diencephalon and the descending pathways of the sympathetic and parasympathetic integrating mechanisms. The principal effects of sympathetic and parasympathetic stimulation are in the motor and secretory responses in the various organs and tissues of the body. Because the change in the original reflex impulse was brought about by activity on the psychic level the psychic factors involved can be said to be the causes of the elaborated responses on the physiologic level. The activities taking place on the psychic and physiologic levels together account for the total phenomenon of the emotional state.

Although it is not known what determines the direction of outflow of emotional impulses it can be said in general that those aroused from a primary feeling of pain and discomfort are discharged predominantly by the sympathetics and those associated with pleasure and comfort by the parasympathetics. The types of response elicited through the two autonomic divisions indicate that parasympathetic control is largely concerned with the conservation and building up of body functions, while the sympathetics are the guardians of the body because the reactions under their control prepare the organism for defense and coördinate activities concerned with adjustments to harmful situations. The parasympathetic division acts synergically with the adrenals. The secretion of these glands (adrenin) acts on the same physiologic functions as the parasympathetic system and in the same manner as stimulation of this autonomic division.

Stimulation of the sympathetic division produces acceleration and increased force of action of the heart, vaso-motor constriction, elevation of blood-pressure, rise in voluntary muscle tonus, bronchodilation with increased pulmonary ventilation, gastro-intestinal motor and secretory inhibition, mobilization of sugar with resultant hyperglycemia, leukocytosis, dilatation of the pupils, increased basal metabolic rate, warm dry skin, and a general alertness of the whole organism. The sympathetic division is composed of the autonomic fibers of the first to the twelfth thoracic and the first and second lumbar nerves and is sometimes referred to as the thoracolumbar division of the autonomic system.

The emotional states of fear, rage, anger, anxiety, worry, painful anticipation and recollection, situational problems, and maladjustment give rise to many of the effects of sympathetic stimulation.

Stimulation of the parasympathetic fibers produces slowing of the heart-rate, increased activity of the motor and secretory functions of the gastro-intestinal tract which favor assimilation of nutrient, broncho-constriction, vaso-motor dilation, contraction of the pupil, sweating, and the conservation of heat with a cold, moist skin. The parasympathetic system is composed of the autonomic fibers in the third, seventh, ninth and tenth cranial nerves and the second, third, and fourth sacral nerves.

The normal stimuli to the parasympathetic system are largely those concerned with the taking and assimilation of food and the internal visceral and somatic impulses which aim to conserve physiologic activity, provide for rest and repair, and coördinate anabolic activity. When emotional impulses acting through the sympathetics are excessive the parasympathetic control is an important factor in readjusting the disordered state.

Emotional response on the physiologic level is ordinarily not prolonged and disappears soon after the removal or cessation of the activating stimulus. It may therefore produce no more than temporary disorders manifested by combinations of the effects listed above. There are occasions, however, in which the emotional state is so acute as to justify the term **emotional shock.** It appears that this is considerably more than a simple quantitative increase in the reactions and involves certain secondary factors which have not been positively identified. A number of theories have been brought forward to explain it. Of importance among them are Crile's[1] *demonstration that traumatizing stimuli (including pure* emotional impulses) when operating without the release of muscular activity produce an acute acidosis with demonstrable histologic changes in the adrenals, liver and brain. Hesnard[2] postulates the formation of cyto-toxins from the disturbances produced in the liver, kidneys and endocrine organs. Pascal and Davesne[3] present the possibility of a psycho-colloidoclastic diathesis which is inborn and manifests itself mostly in those who develop shock psychoses.

It is evident that whatever the mechanism of emotional shock might be, it is not confined to the physiologic level; it is a profound alteration of the entire psychosomatic economy.

Of particular importance to the subject matter of the Category of Psychobiologic and Biosocial Factors are the findings relative to the physiologic changes brought about by long continued or often repeated emotional strain and stress.

[1] Crile, G. W.: Man—An Adaptive Mechanism, New York, The Macmillan Company, 1916.

[2] Hesnard, A.: Rev. de psychiat., 18, 139, 1914.

[3] Pascal, C., and Davesne, J.: Traitment des Maladies Mentales par les Chocs, Paris, Masson et Cie, 1926.

Loss of appetite and indigestion from worry and other forms of mental stress are matters of common experience. The mild emotional stimuli which arise under these conditions unquestionably manifest themselves in physiologic changes in the motor and secretory mechanisms of the alimentary tract. Although the disturbances may not reach the level of conscious awareness of them, the altered physiology not infrequently results in secondary gastro-intestinal disturbance. In a previous discussion consideration was given to effects of disturbances in the timed reactions of the motor and secretory functions involved in digestion. It was pointed out that in the absence of proper timing between the reflex stimuli that start the digestive mechanisms and the time of arrival of the nutrient at the different levels of the digestive tract, functional indigestion was a frequent result. Much of this can arise from poor coördination between psychic stimuli and physiologic response. The stomach which is constantly or repeatedly thrown into motor excitation or inhibition, and whose secretions are similarly deranged by stimuli arriving through autonomic control and which have no real relationship to the need for food, is a non-physiologically functioning stomach. The same applies to the intestine. Delayed or rapid emptying of the stomach may result and the digestive pattern in the small intestine may be markedly altered. Similarly, the colon may be over- or underactive, its absorptive mechanisms may be upset, and normal movement of fecal contents interfered with. It is not surprising to find that psychic factors of even mild types of worry and anxiety are able to bring about gastro-intestinal indigestion, excessive fermentation and putrefaction, and loss of appetite. When such a state becomes persistent because of prolonged mental stress, poor habits, or more definitely psychotic types of behavior, the disorder may lead to far-reaching nutritive defects.

It has long been believed that there was a strong psychic factor in the etiology of diabetes. Although it has not been shown that physiologic disturbances brought about through psychic stimulation of the vegetative nervous system can initiate diabetes there is much in favor of psychic factors being a contributing cause of this disease. Hyperglycemia is a concomitant of sympathetic stimulation and is evidenced in severe emotional states. It appears to result from *sympathetic stimulation of adrenin output and mediation of the* thyroid gland. The heightened blood-sugar level is eventually restored by the action of insulin. This indicates a disturbance of carbohydrate metabolism albeit within the normal limits of tolerance of the mechanisms concerned. The points which have not been cleared up in this problem are first of all whether the excessive demands placed on the carbohydrate metabolism can over-stress the control of the blood-sugar level and lead to true diabetes, and secondly whether such disturbance can act as a precipitating factor

to initiate diabetes when other probable causes of this disease already exist. The former seems unlikely in view of the relatively infrequent incidence of diabetes among the soldiers in the World War in spite of the emotional stresses to which they were subjected. The possibility that psychic factors may precipitate potential diabetes seems more likely on physiologic grounds, and because of the frequent clinical correlation between the onset of diabetes and mental distress of one form or another. It is certain that psychic factors aggravate the course of existing diabetes and the removal of mental stress is an underlying necessity in the management of cases of this disease.

A somewhat similar problem exists in hyperthyroidism. Sympathetic stimulation always involves some degree of thyroid response. It has long been held that emotional shock is capable of converting simple hyperthyroidism into the exophthalmic type.

Less stress is now laid than formerly on the belief that shock alone can cause overfunctioning of the thyroid. Although stimulation of the sympathetics can produce experimental hyperactivity of the thyroid it lacks the characteristics of progressive thyrotoxicosis. Clinicians, generally, believe that emotional stress plays an important part in hyperthyroidism and the observation that this condition is on the increase in modern civilized communities would appear to support this contention. Many of the localized signs and symptoms of exophthalmic goiter can only be explained on the basis of vegetative nervous system involvement and it is not unlikely that the interplay between psychic factors, thyroxin, and autonomic response accounts for the perpetuation of this syndrome.

Owing to almost complete lack of knowledge of the etiology of essential hypertension the rôle of psychic factors can be dismissed with the brief statement that it is held strongly suspect as a contributing cause. It appears that there is some constitutional element which makes the vaso-motor mechanism over-responsive to stimuli of various kinds, of which emotional shock, worry, habitual emotionalism, "nervous drive" may be a few.

Emotional tension is one only of the underlying factors in the production of functional conditions of the heart. In most cases it probably plays a rôle secondary to infection, intoxication, exhaustion from overexertion, prolonged illness, etc. A few clinical cases are recorded of paroxysmal tachycardia, sinus tachycardia and irritable heart (effort syndrome, neuro-circulatory asthenia) in which no cause could be elicited other than an emotional stress of some kind, but such evidence lacks the finality necessary to establish cause and effect.

The functional reactions in the psychoses and psychoneuroses *are the result entirely, or in great part, of psychic processes, but* because they are involved in personality types and alterations of behavior, discussion of them will be reserved for the next chapter.

CHAPTER XLVIII.

THE INFLUENCE OF PSYCHOGENIC FACTORS ON PERSONALITY AND BEHAVIOR.

SOME individuals appear to possess a fundamental inability to retain an even balance between their response mechanisms and the stimuli of ordinary experience. The existence of an inborn constitutional tendency toward this so-called *nervous instability* is quite generally assumed but there is no scientific proof of it.

On the other hand an acquired congenital sensitivity or obtuseness of the psychobiologic mechanisms seems possible on the basis that certain extrinsic factors, operating on the embryo, can alter the biologic qualities of tissues during their developmental stages.

A third possible explanation of nervous instability is that psychic experiences leave their stamp on the psychic mechanisms and incline the organism thereafter toward exaggeration or suppression of responses to normal stimuli.

And finally, it is acknowledged that abnormal states on any level or organization, acquired at any time during the life of the individual, can affect the sensitivity of psychobiologic reactivity.

There are evidences in favor of each of these assumptions and it is likely that their multiplicity is sufficient to indicate that more than one cause is operative in producing the complex reactions included under "instability."

Instability is generally meant to imply that the organism is overtly affected by psychic and other stimuli in such a way that it reacts in a manner out of proportion to what might be expected from the nature of the situation that evoked it. The nervously unstable person is sensitive, jumpy, temperamental, emotional, irritable and apprehensive. It is important to know why these traits appear because when they become manifest in very early life they play a great part in the development of later personality types and behavior, and not infrequently give the color to abnormal nervous and mental states. Unfortunately, the whole explanation is not available in any single school of psychology and must await further research along the lines indicated in the opening statements of this chapter.

It is to be noted that the instabilities (as the term is used herein) involve emotions to a greater or less degree and that at least one of the manifestations (sensitivity) might conceivably rest on a basic constitutional oversensitiveness of the autonomic nervous system. In this instance autonomic response appears to take precedence over conscious behavior and expresses itself before volition can

supplement or inhibit the response; that is, the autonomic system is on trigger-edge. In ordinary emotional overactivity and temperamental states the higher psychic functions seem to play a greater part. This does not imply deliberate exaggeration or submission to feelings but on the contrary, points toward an uncontrollable emotional response in conjunction with fixed associated ideas. Complexes are of this nature.

Feelings and emotion run as continuous threads through every thought and experience and work to the advantage or disadvantage of the organism. If the responsive nervous system through which all ideas, emotions and actions are actualized is hypersensitive, unstable, or inadequate from inborn or acquired causes, the total reactivity will depart materially from the expected.

The factors which arise in the psychic levels of the organism through the interplay of feelings, emotion, and the processes of memory and ideation, or which have their origin in the impact between the environment and the mental functions, are called the **psychogenic factors.** Although they originate on the psychic level their effects are found on all levels of the organism. When their force and import is sufficient to bring about departures beyond the normal average behavior of individuals living in the same social and cultural environment, the psychogenic factors can be accepted as the causative agents of the abnormality.

The average individual is one who is in good physical health and possesses an average intelligence, acceptable emotional control, a sound outlook on life generally, who has ambition and a sense of social responsibility, and is adequately adjusted to the complexities of personal and cultural requirements. Such an individual varies from this level from time to time but never departs far from it. He is neither habitually morose nor elated; does not suffer from marked periods of depression or excitement without just cause; is not too readily led by suggestion or influenced by unsound judgment; his interests are well balanced within himself and his external experiences; there is seldom little evidence that he is dominated by internal struggles; he has the average supply of prejudices, superstitions and faiths of his *time but is not a slave to them. In such a personality* there is near-equilibrium between his psychogenic factors.

When the psychogenic factors are thrown out of balance through inborn limitations, bodily disease, faulty training and education, or psychic and emotional traumatism, the resulting personality traits and behavior depart more or less from the average. In moderate instances of imbalance the total personality may conform in general to the broad concept of normal but there are dominant trends that make such individuals appear different, odd, queer, exceptional or peculiar. They are highly emotional, sentimental or excitable; their interests are too much bound up with themselves or,

conversely, they are too intent on social contacts; they may have satisfaction in things which produce dissatisfaction in the majority; they are represented by the fanatic, the temperamentalist, the recluse, the miser, the unfeeling and cold personality, the martyr, the ruthless autocrat, the grovelling slave, and a host of other "types" recognizable by all.

From time to time individuals are met who combine certain of the above traits in two rather distinct personality types; the *introverts* and the *extroverts*. (The author wishes to warn the reader that the use of these terms must not carry any connotation that they are undesirable stigmata. There is no evidence of any hereditary basis for them nor does it appear that they can be explained biogenetically.) The imbalance of the psychogenetic factors brought about by the unequal development of personality traits (with the help at times of physiologic dysfunctions) appears to be adequate to account for these so-called peculiar types. In general the introvert is a shut-in personality. He is socially unresponsive, withdraws from social contact, and is difficult to understand or rather, it is difficult to make sufficient contact with him, to understand him. The introvert is suppressive and hides his emotions, and is generally of a suspicious nature, harboring silent grudges, jealousies, and desires which are known only to him. He is frequently driven by hidden urges that break out in artistic accomplishments and special skills or he turns leader in a cause which conforms with his inner nature. He is often deeply thoughtful, reasonable and logical but his motives are not necessarily proportionately sound.

In contrast to these, the extrovert is a sociable being. He is expansive to the point of being obnoxious; he is overemotional and excitable but is always so in keeping with the situation that called forth the response; he has strong tendencies toward the formation of confidences and can hold few secrets, not even his own. The extrovert is congenial, happy, philanthropic, gregarious, and good natured; but he is too much so.

Psychology has taken over the terms *cyclothymic* and *schizoid* from psychiatry and applied them to the extrovertive and introvertive personalities respectively. This has helped considerably in the understanding of the cyclothymic and schizophrenic psychoses.

It has been shown above that the content of every situation is composed of psychic elements associated in such a way as to have particular significance through the feelings which they arouse to the welfare of the individual at that time. The individual need not be openly aware of all of the elements at once but grasps the essence of the whole situation in much the same way that he sees a picture in its entirety and understands its meaning without being aware of every feature in it. When at a later

date some occurrence recalls one or more of the elements of a psychic experience, association of those recalled with those of the original experience is such that memory associations reconstruct the earlier situation over again. If the remembered situation originally contained a strong emotional tone and was of great significance to the welfare of the individual, the new situation which aroused the memory of the earlier experience, will be likely to be suffused with the old emotional reaction. Such association constitutes a *complex*. It is immaterial whether the ideas are associated logically or illogically, or whether all or a few of the elements of the original situation are recalled to consciousness. It is only necessary that some element reach the state of awareness for the essence of the situation to be felt and responded to emotionally.

Complexes intrude themselves into all sorts of conscious processes. The general impression is that they are lurking somewhere in the "subliminal mind" ready to make us act in ways which we do not anticipate. On the contrary there is no evidence that they persist as such, but are reconstructed each time that a new situation is experienced which has some element or elements in common with the old. Any question of illogicality in a complex does not necessarily lie in the nature of the complex (although it might) but in the relationship between the ideas or elements in the complex and *those in the current situation which aroused it.*

Normal and emotional associations of ideas make up all conscious thought and underlie most subconscious behavior; they are real psychic events cemented together by memory in such a way that *bidden and unbidden thoughts stream through consciousness and* confuse the purity of every mental experience. When those which arouse a feeling of pleasure comingle with those which are discomfiting, a *conflict* ensues which must be resolved: or one pleasurable feeling may be dominant over another less pleasant, and an unpleasant feeling may conflict with one more unpleasant. If action is demanded in either instance an emotional conflict results. It is obvious that conflicting feelings cannot both be satisfied at the same time. It is here that training of the intellect toward understanding of the logic of situations becomes of great importance. The classical example of a conflict is the clash between the desire of a soldier to stand his ground for the cause he espouses against the desire to run away and save himself. In this situation his natural desire to run away may be stronger than any desire to remain loyal and patriotic; he would respond with little conflict to the strong emotion of fear On the other hand his self-satisfaction (self-respect) might best be gained by sacrificing himself through sentimental attachment to the cause; he might then feel less fear or desire to run away and would solve his situation heroically. The third solution would be for him to acknowledge that fear under such

a situation is normal and that he, with thorough intelligent understanding of his position can do what he thinks best; stand up against the enemy or run away and take the consequences.

The main difficulty with conflicts is that unless they are solved logically they do not stay solved but recur in their original setting whenever some impulse arouses them. Complexes and their resulting conflicts may persist throughout life unless satisfactorily resolved; they cannot be counted upon to be forgotten forever just because they have passed out of consciousness by repression or the imposition of more importunate affairs.

Because complexes always possess the element of emotion they are built up around the common expressions of emotion: fear, hate, love, anger, etc. As examples there may be uncontrollable fear of thunder because of some early fearful experience (actual or hearsay) with lightning and its consequences; a hatred may exist toward an individual because he did (or was said to have done) something highly distasteful and that hatred may be unreasonably transferred to another person who looks like him; a person may be loved for some insignificant trait which was present in another loved one (mother) but which could have no real bearing on the depth of the present affection; early sex experiences may torture the conscience and take all significance out of later sex gratification; repression of early satisfactions in the eliminative functions may remain as shame or disgust at every future reference to anything savoring of elimination.

Unresolved complexes, if uncomfortable, lead to subtle or outward attempts to escape from the conflicts which they arouse, and if pleasant, direct thoughts in a way to linger on them, or action to behave so as to prolong the satisfactions they may bring.

Much is owed to the Freudian school of psychology for the modern understanding of the nature of complexes, repressions, wish fulfillment, dream content, etc., but its insistence on the singular importance of sex in all subconscious activity and the excesses to which it goes to support its contentions cannot be acceptable to anyone who understands the multiple causality of human behavior. Sex does pervade the whole organism, but so does nutritional hunger; fear cannot forever be resolved to a sex basis any more than the multitude of complexes surrounding such unsexed abstractions as economics, politics and mathematics, about which many people have uncomfortable, repressed emotional associations.

The influence of complexes on personality and behavior is profound because their emotional content suffuses every thought and action of everyday experiences in which complexes are involved. This interferes with rational thinking and behavior and is liable to lead to serious irrational activities when the response to the complex tends to be antisocial. It is not to be assumed that complexes

are intrinsically bad and undesirable, or that they possess any mysterious power to make us do what we do not want to do. In the last analysis they are images of past emotional experiences and differ from current experience only in that they are of a private and not a public nature; that is, they have no other qualities than mental and therefore cannot be known to others. Because they are private, complexes would resolve to nothingness so far as their influence is concerned, if their conflict with present reality could be rationalized by understanding.

Habit formation is often referred to as a determiner of behavior, but it is such only insofar as it itself has been determined by antecedent causes. The organism learns most habits, although it is conceded that some may arise through conditioning of unlearned reflexes. When habit is referred to such things as slovenliness, politeness, gambling, early rising, laziness, or good manners, the real significance of the term is lost. These are character traits which have evolved not only through repetition, conditioning, or associated memories but from some one or more of these plus discipline or the lack of it, or to the apprehension of ideas which give values to these behavior characteristics in the individual's pattern of living. The so-called ingrained habit of neatness is no more innate than an excessive desire for sweets. It is far better to look on habit as the result of directed behavior (good or bad) than the director of behavior.

True conditioned reflexes, as opposed to the above, are real habits. They rest on a purely physiologic basis and owe their effect on behavior to the fact that the conditioned responses involve psychic processes. For example, the need of some people to defecate on arising in the morning is conditioned by the act of rising, the thought of food, the preparation of the toilet, and the act of moving about. Conditioning is also seen in more actively mental states as in some of the revulsive reactions and so-called instinctive tendencies to avoid harm. Insofar as these indirect responses recur repeatedly to similar situations they may be called reflex habits and so alter behavior, but the psychic component is always present and on occasions is so concerned with other elements in the situation that it may overcome the reflex tendency entirely.

CHAPTER XLIX

THE RÔLE OF PSYCHOGENIC FACTORS IN THE ETIOLOGY OF MENTAL AND NERVOUS DISORDERS.

Most of the attention to mental diseases in the past centered on their description as disease entities. This was the natural result of the enthusiasm for scientific classification but doubt has been thrown on the reality of some of the categories and new criteria have been set up in an attempt to construct an objective science of psychiatry. The result has been to change the concept of mental diseases from conditions of static entities to dynamic processes which result from effective causes operating on flexible psychic functions so as to disturb their equilibrium more or less permanently. It has brought the functional disorders to par with organic nervous diseases by according them equal causality through disturbances of normal equilibria. Mental disorders have a Natural History which includes knowable etiologic factors and an objective pathogenesis.

Among the etiologic factors which operate to the detriment of the psychobiologic mechanisms are the psychogenic factors—those psychic responses to stimuli originating in the organism or the environment which when aroused can affect the psychobiologic processes because they are part of them. Worry, for example, is a psychogenic factor; it is neither inherent in the organism nor in the environment but appears in the organism in response to certain relationships between it and the external situations; the result, as worry, enters into the psychic processes of the organism and disturbs it on the psychic and physiologic levels as shown by insomnia, fatigability, loss of appetite, irritability, inability to concentrate and so forth. Worry and other psychogenic factors are therefore not primary etiologic factors but as end-processes of antecedent situations are able to institute their own chain of consequences and so act as adequate causes of mental and nervous disorders.

Increasing importance is being placed on the part played by psychogenic factors in the etiology of the psychoneuroses and psychoses. As it is not the purpose of this book to undertake a review of the etiology of the individual mental disorders but to present the broad outlines on which their etiology is based it will be sufficient to present a few illustrative examples.

Hysteria is a typical psychoneurosis which has been well studied from the etiologic approach. It has been described as a malady of the imagination. This is a serviceable description if it is remembered that no etiologic implications are to be read into it and that it is

only a statement of an apparently basic phenomenon underlying many of the manifestations of hysteria. Why the imagination is so excessive and reveals itself in the outward simulation of so many disease states is not known.

The psychogalvanic reflex response in hysteria points to some disturbance of the affective mechanism. The galvanometer fails to respond in the hysteric even when the outward response to noxious stimuli appears greater than in a normal person. If there is actually a defect of the affective response mechanisms in hysteria which antedates the clinical onset of this disease its nature and cause remain entirely unknown. There is little doubt that there is a dissociation between the discriminative powers and the physiologic response to discomfiting stimuli. Furthermore it is not questioned that the psychogenic factors play the major rôle in producing the manifestations of hysteria. The simulation of disease, the advantage of illness motive, the phantasies, exaggerated statements and lies, the supreme egoism, and the sham emotionalism of the hysteric are all psychogenic phenomena; they are an inextricable tangle of ideas, feelings which cannot be satisfied organically, memory images jumbled up with present reality, and a hypersusceptibility to suggestion. Without outward help, the hysterical subject is hopelessly entangled in a psychic web of his own spinning—why he is, remains the central problem in hysteria.

Psychic trauma is a frequent concomitant of the onset of the psychoneuroses and probably bears an important causal relationship to it. In a susceptible subject such psychic disturbances as sudden fright or bereavement may precipitate a traumatic hysteria, hysterical overindulgence in emotional grief, or an anxiety neurosis with complete "nervous breakdown." In these conditions psychogenic factors are obviously directly concerned with the disordered state.

In the major psychoses (manic-depressive or cyclothymic psychosis, and dementia præcox or schizophrenic psychosis) the psychogenic factors may not be obvious as causative agents but they constitute a major part of their manifestations. Where the psychoneuroses involve limited changes in the personality because of the dissociation between discrimination and the expression of feelings, *the personality and behavior of the psychotics show changes in the* total personality which involve its feelings, emotions and intellect. Demonstrable organic defects which might underlie the development of the psychoses are generally wanting, and there is seldom any outstanding psychic event to which the onset of the disorder could be attributed. The whole psychic organism seems to give way without reason and it is because of this that the major psychoses are called "biogenic psychoses." The term is obviously a poor one because the implications of spontaneity cannot possibly be upheld.

The cyclothymic and schizoid characteristics of manic-depressive psychosis and dementia præcox bear striking resemblance to the extrovert and introvert personalities respectively, or as Devine expresses it, "certain psychoses (will) figure as caricatures of certain normal types of personality." It is a temptation to believe that the extrovert will develop manic-depressive reactions and the introvert shizophrenia if the necessary conditions for the development of these psychotic states are present but there is no proof that this is so. Studies on the past histories of psychotics tend to confirm the possibility of such a relationship but it may amount to no more than a similar observation on other mental derangements (delirium, intoxication, etc.) that the normal personality tends to color the abnormal state.

In general it may be said that the psychogenic factors *may* precipitate at least some of the psychoneuroses, *may* underlie the direction of development of the cyclothymic and schizophrenic psychoses, and partake in the characterization of all of these conditions. When a psychoneurosis or a psychosis is once established the psychogenic factors, by virtue of the part they play in distorting the relations between the individual and his environment, may be the important perpetuating factors standing in the way of recovery.

CHAPTER L.

THE DEFENSE AGAINST PSYCHOBIOLOGIC AND BIOSOCIAL FACTORS.

The prevention of disorders of the psychosomatic functions must rest primarily on assuring that the infant will be born with an adequately functioning psychobiologic equipment, and the obstruction of all postnatal factors which can affect this equipment harmfully. It involves therefore every effort favorable to a good inheritance and the prevention of acquired physical and mental defects which might result from the action of effective causes in every category of the etiologic factors of disease. Among these categories, that which contains the psychobiologic and biosocial factors is of greatest moment to the welfare of the individual insofar as his psychic or mental integrity and his ability to adjust himself to his social environment are concerned.

The manner in which the psychobiologic mechanisms respond to external situations and internal stimuli, as evidenced by conditioned *reflexes, habit, learning, memory, and suggestion, makes it possible* to direct responses by deliberate training. What limitations exist are probably due to inborn susceptibilities to react in particular ways and degrees and to acquired susceptibility or obtuseness to stimuli of various kinds. Within these limitations training is the best defense against undesirable behavior. The methods of training will therefore constitute the present approach to child guidance and mental hygiene.

TRAINING IN THE NUTRITIVE AND ELIMINATIVE FUNCTIONS.

The fundamental needs of the organism must be met be giving them every opportunity for normal expression. This must begin immediately after birth. Hunger for nutrient and the desire to eliminate are the first evidences of disturbances in physiologic equilibria which require overt behavior for their restoration. It is imperative that these needs be met satisfactorily. Pediatric *teaching recommends regularity of feeding on a physiologic basis* and not on the whims of the mother or nurse.

This rests on the recognition that the physiology of digestion and assimilation in the infant can be served best by regulated feeding because the demand for food and the response to it involves levels of activity higher than those of simple physiology, and regular, orderly feeding assures good eating habits and physiologic condition-

ing. It is an attempt to organize the digestive patterns in keeping with a well ordered daily régime. Although much more latitude may be allowed in this regard with increasing age the same principles are involved throughout life. There are certain age periods where good eating habits are of particular importance. The first is in the young child of pre-school years who shows strong tendencies to discriminate between articles offered it. These tendencies result largely from interference on the part of the mother or nurse in the normal reactions of the infant and young child. It has usually been unduly cajoled, disciplined, or spoiled, and has found some value to itself in making a fuss over its food. It is not too much to say that normal infants can and will eat anything fit for infant consumption. There is no inborn aversion to spinach or cod-liver oil. The unspoiled, well-trained infant will be no feeding problem in the pre-school years. Unfortunately there will always be difficulty in maintaining this ideal because of the interference of factors which may be entirely unrelated to eating, such as the poor examples of other children and adults, unwise attentiveness to the child for either its good or bad behavior, fatigue, excitement, and distractions. These influences must be approached from other angles.

Adolescence presents additional problems in feeding because of the intrusion of outside interests and the increasing freedom accorded the child which it is not long in taking advantage of by eating away from home and between meals.

As this is an age of altered physiology and multiplying activities adequate nutrition is essential but difficult to attain. The enthusiasms of youth are unchecked by normal fatigue and the tendency of the adolescent is to go on and on and catch its rest when it can. Appetites fail, become perverted, or go to the extremes of satisfaction; they lose their proper relationship to demand.

Although bad eating habits are quite general all through adult life and lead to poor health of many kinds most people can restore the insults to digestion if they will. With them it is a matter of conscious readjustment within the possibilities of their mode of living. They may have particular desires in the way of food and may arrange their meals as they see fit but none of these habits are necessarily incompatible with good digestion. It is more a matter of what and how they eat, than when.

The point of greatest significance in the habits of eating is that mental attitudes play a greater part than any other factors. This psychic factor is amenable to control, and requires nothing more than the inculcation of good habits in infancy and early childhood, and rational understanding of the elements of nutrition in later childhood and adult life. The satisfaction of nutritional needs is a pleasurable response and should not be allowed to be diverted by things unpleasant. The infant must not be irritated by faulty feeding,

the young child must not be made uncomfortably conscious of how and what it should eat, the adolescent should be taught and not forced to understand its nutritional needs and how to supply them, and the adult should eat calmly, wisely and not too well. Psychic factors alone have the power to make or ruin good digestion and the first law of good eating at all ages is to partake of a physiologic diet physiologically.

The greater part of appetite is not based on physiologic needs but is the result of acquired attitudes toward eating in general and enthusiasms for special articles of diet. Too often, esthetics have largely replaced natural desires. The advertisements for foods cater to the attractiveness of dishes, and confuse the appearance of foods with their nutritive value. The counter-attack on food propaganda should consist in offering the child a varied diet of common foods, well prepared and served in such a way that they will not be non-appetizing. There is such a thing as presenting food so that it takes the appetite even to look at it, and unquestionably some aversions to particular foods result from this fact. But overemphasis on fancy cooking and serving is also bad.

The basis for most overweight is excess food for the age, height and sex of the consumer. There is a strong mental contagion in family habits of eating, and where the elders of the family make too much of food, with undue emphasis on palatability, the children are prone to overeat. The overconsumption of sweets is a frequent concomitant of overeating generally and is an acquired habit. The correlations between obesity and hypertension, and overweight and juvenile diabetes are indications that the bad habits of eating which lead to excess weight should be prevented.

From the time that the first bowel movements of the infant have been inaugurated, the autonomic reflex control of the colon and rectal sphincters becomes automatically associated with the entrance of food or secretions into the upper intestinal tract. This early need to eliminate feces is entirely involuntary and must be satisfied whenever the reflex stimulus to defecation is aroused. The passage of food into the duodenum stimulates the colon through the duodeno-colic reflex and as the bolus reaches the rectum and sets up a pressure on its walls the defecation reflex is brought into activity with contraction of its musculature and relaxation of the rectal sphincters.

In early infancy, bowel elimination is entirely reflex and involuntary but cortical connections later make it possible for the simple reflex act to be controlled. It has previously been pointed out that the gastro-intestinal responses to hunger and the intake of food are readily conditioned to react to stimuli not necessarily connected with feeding. This conditioned response stimulates the colonic and rectal reflexes and causes loss of the purely adaptive response to

a real need; it is caused to act for the reception of food when there may be no food. To combat this, voluntary control of the defecation reflex is instituted. Whether this is true conditioning is not settled but it appears as though the reflex act becomes conditioned *not* to act at any and all times that it may be stimulated, but only at such times as voluntary control permits or forces it to act. It is evident that the early establishment of good bowel habits is imperative in order to regulate elimination in keeping with feeding and other daily routines.

Emptying of the bowels is one of the pleasurable conservative functions of the body and represents a restoration of equilibrium which is necessary to continued good health. The infant who is trained early to regular habits of defecation is usually a happy infant; it is seldom subject to constipation unless other important factors are involved. As the baby grows into childhood the act of defecation is not only pleasurable but interesting and the young child not infrequently exhibits animal-like curiosity in what it has passed. Under no conditions should the pleasurableness of elimination be interfered with and no attempt should be made to discourage natural interest in it. On the other hand undue interest should not be encouraged. Every effort toward training in good bowel habits must center on the regularity of defecation and the institution of measures to make the act comfortable and agreeable instead of something to be put off because of discomfort, either physical or mental.

Bowel training should be continued throughout childhood because accessory factors may enter to upset the well-formed habits of infancy. This is particularly true of the school age where the rush to get off in the morning and the intrusion of play interests are liable to take precedence over regularity of elimination.

In both the child and the adult, social factors frequently interfere with opportunity and desire for bowel action. Embarrassment often causes the act to be put off until all desire has passed and this is likely to end in the accumulation of hardy dry feces and dyschezia. Under ordinary conditions no such urgency should arise if the bowels are habitually emptied at more convenient times.

Regularity of bowel action is one of the best ways of forestalling intestinal neurosis when other conditions necessary for the development of this state exist. Spastic constipation on a neurogenic basis is more likely to occur in those whose intestinal activity is already disturbed by irregularity and difficulty in defecation.

Complexes which have a nucleus of emotional attitudes toward the acts and products of defecation can best be avoided by training children intelligently in the necessity for healthy activity of the bowels, and the inculcation of a sensible attitude toward the products of elimination. Never should shame or embarrassment over

eliminative acts be allowed to culminate in prudery and sensitiveness toward the thought or mention of excreta and elimination, or to develop into ideas of nastiness connected with them.

The mechanisms of urination are very similar to those of defecation and in early life the two are closely associated through the spinal mass-reflex act in which the child passes urine, empties the rectum, sweats, and reflexes its limbs all at the same time. Even with training this involuntary association continues for years but at about the second year cortical control is able to dissociate the acts of defecation and urination so that the young child voids urine without passing stool. Under certain circumstances the act of urination persists involuntarily as *enuresis, or bed- and clothes-wetting.* Although a few cases of enuresis are probably due to organic factors such as adherent prepuce, vulvo-vaginitis, gastro-intestinal disorders, cystitis, pyelitis, etc., the great majority depend on primary psychogenic factors. From late infancy and early childhood the act of urination has been associated with many personal and social reactions, and these children are undoubtedly far more aware of the importance which the adults place on the time and way it is done than parents and doctors realize. It must be remembered that a primary feeling of satisfaction accompanies the act and that this is of first importance to the child. The benefits, both physiologic and psychologic, *may far outweigh any consequences* of the act even though the latter may be disagreeable. Furthermore, bed-wetting and clothes-wetting draw attention to the child which is exactly what it wants. It is claimed by some that enuresis is a protest reaction. If this is true it is protest not so much against punishment as against the distraction of the parent's interest away from the child.

Nocturnal bed-wetting may persist to and beyond puberty without any apparent organic cause. It has been noted that elimination *in these cases occurs during profound sleep and the suggestion* has been made that in this state cortical subconscious control has been practically eliminated and the reflex act occurs under stimuli which arise from endogenous foci of irritation such as a full rectum, and sacral congestion from posture in bed, or from exogenous stimulation from too heavy bed clothes, binding night clothes, or too great body warmth. Although this might be true the same factors exist with non-bed-wetters, and it appears that these may be effective causes only when the reflexes have previously been conditioned by psychic factors. It is certain that the bed-wetter does not deliberately want to do it and probably cannot help it.

Prevention of enuresis is primarily a problem of training. As in defecation, the act of urination should be kept as free of psychic components as possible. It must be remembered that the organs of urination are closely associated with or are part of the genitalia

and this allows additional interests to insert themselves into the use of these parts. The child must be taught by ignoring it outwardly and training it deliberately that urination is normal, unemotional, and can be done without fuss or punishment.

TRAINING IN THE CONTROL OF FEELING AND EMOTION.

The affective state or feeling which is aroused by the content of every situation is frequently so subtle and unobtrusive as to be entirely overlooked or ignored. Thus there are hundreds of psychic events which occur every day to which the organism seems to be entirely passive. There appears to be so much accustomedness to the ordinary experiences of daily living that they lose all vividity. And yet similar experiences under other situations stimulate or depress, please or displease, and give rise to conscious feeling toward them. To the city dweller a skyscraper is a commonplace, but to the country visitor it is awe-inspiring; the sight of blood to a surgeon is a call to intelligent action, to many it is so disturbing as to cause them to fall into a faint. On the other hand the city dweller may have marked affective response to the beauty of the country, and the surgeon may be seriously upset emotionally by suffering in his own family.

It is the feelings which give vividness to life, but excessive affectivity to things and events which are unimportant is a waste of energies and a potential danger to health. Common expressions of this tendency are "he gets all excited over nothing" and "she is so highly impressionable." The two harmful effects of these high-strung feeling tones are interference with intelligent thought, and the intense responses they arouse in the physiologic mechanisms. No one can be completely logical and clear mentally who is kept keyed to a high pitch over non-essentials. Sir William Osler contributed an essay on the subject of equanimity which still stands as the paradigm of good advice on how to meet life's situations calmly.

Because emotionalism involves feeling, association of ideas, inhibition, physiologic activity and attitudes toward the situation, the degree of emotional response can be controlled to some extent. Although there may be little possibility of controlling the immediate response to highly acute and disturbing situations that startle, frighten, cause mental anguish and so forth, the perpetuation of the response after the acuity of the situation is passed can readily be controlled. The unnecessary responsiveness is a learned reaction and because of this is open to training in the opposite direction.

Effective training in emotional response is best obtained in infancy. The infant is concerned only with itself and soon learns to take advantage of every situation which is favorable to its welfare. The mother and nurse encourage it by their own emotional

response to its needs, and go beyond the essential satisfactions by showering it with attentiveness and sentimental gushing. The baby responds and perpetuates the cycle for its own content. On the other hand the infant meets with disappointments, frustrations, and painful feelings that result from the orderly arrangement of its *régime*. If *instead of permitting the infant to develop tolerance* by allowing it to express itself forcefully, which is harmless, the attendants break down the disciplines because of their own emotional discomfort, the baby again soon learns the value of its behavior. In both instances associations are formed between situational elements, emotional response, and personal gain and a satisfying habit pattern is readily developed in the first case by prolonging comfort and in the second by curtailing discomfort. Such habits of satisfaction at this age will be augmented later when the acquisition of new ideas supplements the capacities for self-indulgence.

Very young children may show all shades and degrees of emotional response: they may be phlegmatic, self-contained, mildly responsive to justifiably exciting and depressing experiences, oversentimental, worrisome, afraid, excitable, petulant, or give way to emotional outbursts out of all proportion to the inciting stimulus. These reactions are usually not casual occurences, but are repetitive and put a stamp to the whole behavior and personality. The child can thus be wrongfully stigmatized as sensitive, overaffectionate, apathetic, unresponsive, temperamental, irritable, impulsive, or ill-tempered. These are not innate temperaments but each has developed in response to a personal motive which attained a high value in the child's total satisfactions. These temperaments *per se* would carry no harmful consequences to the individual if the expression of individuality was all that mattered. But unfortunately other individuals are concerned and the child cannot be left to express itself in excessive emotionalism and still expect it to adapt *and adjust itself to a social environment that may not look at the* situation from the same point of view.

Analysis of children's behavior shows that excessive emotional responses are not simple responses to the situation but are normal, acceptable reactions supplemented by powerful, willful, and deliberate psychic elements surrounding a central idea. The idea assumes greater importance than the cause of the disturbance and *the child backs it up by strenuous suppression or augmentation.* The result, when repeated over and over, and become habitual, produces a disharmony within the affective life which becomes an individual and social liability.

The growth of ideas around emotional reactions in early childhood is the natural result of exposure to accumulating experiences which have an affective value and consequently produce some

degree of emotional response. Insofar as these experiences are normal and natural and are therefore stimulating and exciting and arouse interest and curiosity they are good influences; they are the dynamos which charge the personality with healthy responsiveness. But if the experiences are constantly painful, uncomfortable, and unsatisfying the attempt to evade or change them will call forth undesirable emotional responses. Such experiences are occasioned by contacts with nagging mothers, irritating brothers and sisters, disciplinary fathers, marital discords between parents, and by overemphasis on neatness and gentlemanly and ladylike deportment, oppressive religiosity, quarrelsomeness in the family, mental disorders in members of the household, and a general environment of tenseness, anxiety or fear.

Occasionally a child will cultivate an emotional reaction for the sake of the emotion alone. It may be likened, with reservations, to self-abuse. In these instances experiences with the emotional reaction accompanied by tenseness of the body, flushing of the skin, accelerated heart action, and other visceral responses, may have produced a generally pleasant sensation akin to intoxication. By fastening its attention on the result rather than the cause the child is enabled later, in less important situations, to experience the same exhilaration over again, and this may become habitual. Or the child may become introspective and be able to reproduce the reaction through memory or imagination. It begins a phantasy existence and receives the same joys from unreality as from actual experience.

Another source of emotionalism is found in the complex. This has been more fully described in the preceding chapter and it only remains to be pointed out that a complex is not an inevitable consequence of emotional experience. It only occurs when a permanent bond is formed between the feeling-tone, emotional reaction, and the idea or ideas associated with them. It is not a true habit or a phantasy reconstruction but is an association between new and old situations, colored by a strong emotional tone.

It is clear that the prevention of emotional excesses is possible by training the growing child. The most important feature of the attempt must be to order the child's environment so that it is not subjected to excessive or repeated emotional discords. There are many practical difficulties in the way of attaining this end but they are seldom insurmountable. It involves social readjustment and instruction of those in contact with the child how to behave in its presence and how to handle it. Occasionally this may have to be extended to the psychiatric treatment of deranged members of the family. As to the control of the child itself it is only necessary to understand that it behaves as it does for good reasons of its own. It is only as these reasons can be elicited that any intelligent under-

standing of the child's problems can be had and the adjustments made.

It was remarked earlier that the unspoiled infant generally becomes an unspoiled child. Such a child even in a disturbing environment usually does not go to excesses of emotion unless it is encouraged to do so. Good mental hygiene for the normally behaved child is therefore to encourage fortitude, make little of occasional outbursts, satisfy necessary responses to prevent undue frustration, and for the household members to realize that their example is more often the determiner of the child's behavior than *any tendencies in the child itself.*

Complexes are best prevented by intelligence and understanding, and since these are based on the apprehension and use of sound ideas, good results can be expected if sound education is started when ideas are being grasped. The emotional content of complexes is therefore as preventable as complexes themselves.

In conclusion it can be stated generally that abnormal expression of the emotions is acquired and results from predictable causes. To avoid it someone must take intelligent precautions to see that development is natural and unforced, and that major disturbing elements in the environment are adjusted before the infant enters *too deeply into the social milieu. The parents alone are in the* position to undertake this responsibility and this means that they must be understanding, sympathetic, and firm with the personality growing under their charge.

Emotionalism in the adolescent and adult can be prevented and, overcome by the application of more intelligence. Unless there is an underlying defect of the affective mechanisms, as is possible in hysteria, the person who has reached the age of discrimination and understanding, is open to intelligent self-analysis and deliberate control over the affective responses. The least that can be expected of an otherwise adequate normal individual is the exertion of sufficient *self-control as not to take undue advantage of spontaneous* emotional reactions by exalting them to the same level of values as he applies to the really important aspects of life.

TRAINING IN THE USE OF THE INTELLECTUAL FACULTIES.

The intellectual faculties permit the human organism to act in harmony with or in opposition to situations presented to it, and in so doing create and solve problems of adjustment that the human shares with no other creature. Although he may instinctively satisfy many of his fundamental needs the human being will not rise to the full accomplishment of its capacities, and may not even survive to do so, unless the intellectual functions develop to a high degree of perfection. Intelligence is the only way out for the human

race. Because the development of knowledge and the instruments which man uses have grown up together it is becoming increasingly more difficult for the individual to adapt himself to the conditions of his man-made environment unless his knowledge is commensurate with his culture. Unfortunately man inherits only the capacity to know and not knowledge itself. For this reason he must learn, for if he fails to do so, the consequences to his welfare may be serious. To prevent such an outcome some responsible authority must direct the use of his intellectual functions when he is young, and the direction must be toward the greatest usefulness in the society into which he is born.

With the exception of the mental defectives all men are highly educable. (They may lose some of their educability through acquired defects but these failures constitute an entirely different problem.) The biopsychic equipment is generally adequate to actualize all of the current ideas of the time so that all that is necessary is to present ideas to it in such a way that the perceptions from without are comprehended within, and to encourage the relationships which the mind recognized of its own accord between the data of experience. A homely example of a conception grasped by the deliberate presentation of an idea is the baby's eventual understanding that it can use the spoon for eating, and an instance of a self-discovered idea is seen in the baby's reach for the teething ring suspended above it but which it had never handled. The idea comprehended in each case immediately becomes a datum of learning and is a generalization which can be applied to innumerable situations.

Intellectual training must aim toward the comprehension of ideas that will be good for all time and on all occasions. Since the growing, moving, marrying, and reproducing organism, and the environment at different times and places are both in a state of continuous change, it is inconceivable that any one individual could learn the details of all possible situations and experiences. But it is possible to imagine one with all the necessary intellectual tools to understand, examine, and relate the sense data of all of his experiences and to know what to do with them. It is therefore understanding of the true relationships between the data of experience that constitutes real knowledge, and it is the application of this knowledge to the elements of a situation that gives the stamp of intelligence to human thought and action.

True education like every other purposive training begins in infancy. No one knows when an infant first gets an original idea but it must be taken for granted that it does so early. From the earliest months therefore it should be presented with situations which are as nearly true as possible; to deceive the young child is to encourage the development of many of the very qualities it is most

desirable to prevent. This is not to say that it should not be told fairy stories. The toddler lives in its self-made land of make-believe as soon as it has learned the necessary elements out of which to manufacture its imaginations. Fairy tales, myths, and legends serve a useful purpose in logic, the premises may be all wrong and the deductions pure fiction but the child has a happy faculty of *hanging the elements of its imagination in a fairly logical order.* What should not be done in story-telling is to permit the intrusion of emotional reactions of harmful degrees. Many superstitions, beliefs, and prejudices in the adult are the result of impressions gained from bed-time stories with strong emotional appeal.

Formal education must be more than amassing facts and developing special skills. These are useful and necessary elements of training but they are not the core of intellectual achievement. The essence of the thing to be strived for is understanding. *Understanding is the highest intellectual accomplishment. When it can* be acquired toward the important situations of daily living there *will be fewer difficulties in meeting them intelligently and less* opportunities for serious maladjustment. Sound understanding of why certain happenings occur robs them of most of their emotional content. The fear of water for example, is not an essential response to being on the water. Even though the passenger in a small boat cannot swim there are probabilities that can be reasoned out that make it unlikely that he will be called upon to swim. Emotional reaction can similarly be held in abeyance by sound ideas in situations where there is threatened harm, unaccustomed and awe-*inspiring sights, clamor, noises, etc. Intelligence can prevent* over-emotionalism and sentimentalism for their own sake. If constantly *applied, easily, naturally, and eventually subconsciously, good* intelligent attitudes are the surest way toward a healthy equanimity.

A few special applications of intelligence will be given because of their particular usefulness in prevention. Understanding of the nature of foods is necessary for good health. It has been pointed out that there are no specific appetites created by physiologic needs for particular food elements other than water. On the other hand there are desires for special foods which may run contrary to needs. The majority of people eat without any knowledge of their food requirements and go through life with far from optimal diets. It is only recently that the fundamental principles of the balanced diet have become generally known but where they have been applied health has been improved and innumerable cases of deficiency diseases have been prevented.

Prevention of disease will benefit immeasurably when the public *acquires a clear understanding of the nature of disease and the* virtues of cleanliness, is careful in the treatment of wounds, avoids *self-medication, accepts the claims of advertisers with caution,*

practices personal hygiene and care of the teeth, eyes and ears, and *adopts discretion in the use of intoxicants and stimulants.* These virtues are learned and must frequently be maintained against strong odds. Only a firm conviction of their value, based on reason, can combat the superstitions, prejudices, falsifications, and emotional attachments that work in opposition to them.

Awareness of the elements in a dangerous situation implies the application of intelligent thought to the probabilities of danger. Driving a motor car through traffic is such a situation. If a driver is aware of the power of his car and its potentialities and knows how fast he can drive it with safety and how quickly it can be stopped; if he has acquired a sense of anticipation toward what other drivers about him are likely to do next; if he knows the traffic regulations and intelligently respects them; if he has further anticipated trouble by seeing that his car is in good condition before starting out; if he realizes that he can't talk and be distracted and keep his mind on his job at the same time, that driver will seldom get in serious trouble. The same applies to the pedestrian crossing the street, the workman at a circular saw or on a high scaffolding, a person with pain who reaches for a sedative in the medicine closet in the dark, and everyone who becomes involved in situations where intelligent precautions can be used in the prevention of accidents.

TRAINING IN THE APPRECIATION OF PERSONAL VALUES.

There is hardly any aspect of personality less predictable than the personal values or so-called character traits of an individual. Whereas the emotional and intellectual characteristics may be seen to unfold and reveal themselves in outward behavior the personal values remain largely hidden in the private inner life. They may participate in or show themselves in behavior but it is difficult to know in any given case just what part they are playing. For example, it may be assumed that a certain person is honest because he has always appeared so, and yet there may be little real honesty in him; what he shows is false, expedient, and valuable to his own interests.

Personal values are fundamentally built-up behavior patterns which have a purposeful meaning to the individual. They are *neither simple intellectual responses to situations nor deliberate* attempts to hold on to pleasant situations or to get rid of unpleasantness. They are compounded of both of these, frequently with considerable emotional tone, plus a far reaching teleological significance to which a high personal value has been attached.

Their origin is thus hidden in the whole developmental process and it is often impossible to explain how they came about in any given case. Frequently, they arise contrary to all expectations and

in the face of a general environmental influence that would seem to be more likely to develop character of a different kind. Nevertheless there must be certain favorable or adverse conditions in the environment with which the whole personality has to deal, and in so doing, evolves an attitude toward them which aims toward satisfaction. The apparent secrecy with which some character traits are surrounded is evidence of their purposiveness, for to reveal them too clearly might defeat their purpose. Those in which an advantage can best be gained by overt expression do not require indirectness but may be revealed openly and honestly even though they may not conform to the opinions of society.

Character training is an attempt to inculcate those traits which society brands as good and to combat those designated as bad. Inasmuch as what society wants is not necessarily what the individual thinks and wants it is obvious that without deliberate training it will be largely a matter of chance that the character traits will conform to social acceptance. Training is most likely to be successful in early childhood. Because many of the character traits depend on learning, positive training should be applied in this period when learning is most active and new experiences make the deepest impressions. The young child's personality development is a personal experiment; it is trying itself out under all kinds of conditions and circumstances. Successes and failures follow each other rapidly, and the young mind is unable to adopt any one attitude which will bring success most of the time. But eventually it evaluates some one or more trends which it finds useful and begins to crystallize them into purposeful lines of thought and action.

The terms applied to the particular character traits unfortunately do not bring out their full significance. Thus timidity is looked upon as a negative virtue and implies the lack of its opposites, aggressiveness and courage. But from the point of view of the timid child it is a wise trait to cultivate. Somewhere at some time in its development the child has met repeatedly with situations with which it could not cope without retreating. But the very retreat saved it. By adopting a general attitude of retreat it makes it appear to others as though it were afraid and it is called a timid child. The child on the other hand is inwardly happy in its success in evading discomfort and inferiority. This important conception is owed largely to the Adlerian school of psychology. Cautiousness is a little less retreat than timidity; the child is still willing to experiment but tries out the situation first. Courage is the positive, aggressive phase where straightforwardness backed up by self-assurance, or false courage supported by bluff, is found to succeed often enough to serve the purpose.

A child is often spoken of as inherently truthful. There is no inborn trait of truthfulness or any other character. The truthful

child learns truthfulness as it learns everything else, but later, when reason and logic are understood and applied, it may rationalize its unreasoned truth and adopt it as a way of life. In its beginnings the child adopts accuracy in recounting its exploits because it brings satisfaction to do so. Another child in the same environment may be as habitually untruthful because its own personality does not fit into the environment as satisfactorily when it tells the truth. Both of these children are being honest with themselves and that is all that concerns them.

There are a number of traits that possess in common a feeling of superiority. They are, in a more or less ascending scale of intensity (but not of value): initiative, ambition, pride, vanity, conceit, impudence and arrogance. In themselves they are neither good nor bad, but they have different social values. To their possessor they are all of value, and to different degrees satisfy the fundamental trait of all organisms, which is the desire to succeed (or the need to succeed if expressed biologically).

Their opposites, the inferiority traits are: modesty, lack of ambition. and initiative, lack of fortitude, dependence, overobedience and servility. Here again the traits do not conform to social value. Obedience is ordinarily given a high positive value by society, but the overobedient child is a non-aggressive child and frequently exhibits an almost negative personality.

The aim of character training is to cultivate those traits which seem to be most desirable for the individual in the circumstances in which it is reared until it reaches the age where it can discriminate. This is justifiable *if* assistance is given later in its attempts to discriminate. It seems to be untrue that the character traits of early life invariably become fixed for all time. An untruthful child can be taught to become truthful, and an ambitious one can have all ambition "knocked out of it" by poor training later. Parents, teachers, and guardians can do no more than encourage by precept, example, and teaching, what they believe are the best traits for their charges, and to support this effort by presenting the learning child with sound ideas which it can apprehend and apply to itself as its basis of success.

TRAINING IN SEX NEEDS AND SATISFACTIONS.

One of the fundamental purposes of the individual as a unit of society is to serve as an instrument for the propagation of its kind. But it is an incomplete instrument because the perfect fulfillment of its use involves the coöperation of its complementary unit of the opposite sex under the bisexual plan of human biology. From this it follows that the individual must participate in the functions of his social environment insofar as this is necessary for the biologic ex-

pression of his sex needs. And furthermore it is only by this expression that he can normally and completely fulfill his highest biologic function.

Taken in its entirety sex pervades the whole organism as a primary physiologic hunger that arises from disequilibrium in the sex mechanisms—gonads, sex organs, erogenic tactile sensations, reflex arcs, the integrations of the senori-motor nervous system and endocrines, and the higher psychic functions. It is useless to talk of sex simply as desire and gratification or as part functions like love, eroticism, sensuality, and a specific sex energy (libido), or to consider as entities such conceptions as self-love (narcissism), parent-child attachment (œdipus and electra complexes), homosexuality and other so-called perversions—these are all qualifications applied to particular expressions of the sex-need as they appear at certain levels of the sex functions, with or without participation on the social level.

There are two main divisions into which sex-needs and their resulting satisfactions can be considered: (*a*) within the organism (personal), (*b*) between organisms (social, heterosexual).

In the infant, and in the child up to the age when the gonads become functionally active sex is entirely personal. The sensations arising from erogenic tactile areas of the body, particularly those of the lips and genital regions are very nearly the sole expressions of sexuality in the infant and young child, but not completely, because at a very early age psychic components enter into the expression, as revealed by emotional reactions associated with irritation or manipulation of the erogenic areas. The whole reaction may be likened to a closed electric circuit—the impulse arises at one point, is transferred throughout the mechanism, and its energies are all expended within the mechanism.

In the pre-school child sex-feelings still arise from tactile stimuli but they are augmented by more deliberate attentiveness to them. This results in the child showing more interest in itself and its feelings and a corresponding attempt to obtain the maximum of pleasure from them.

The attentiveness comes from awareness of the sensory areas brought about by urination, cleansing of the genitalia, kissing and caressing. Consequently the child continues thumb sucking and handling of the genitalia and eventually anticipates the touch of the mother or nurse and others who may care for and fondle it. Any element of attachment to the parent, if due to sex factors at all, is nothing more than consideration of the parent as the stimulating agent—most of the attachment is on the basis that the parent is the source of nutrient, the protector, the satisfier on all other levels of behavior.

Unquestionably, this is the great conditioning age but the extent

of sex conditioning is very limited and almost entirely confined to the tactile senses. Any sex associations which appear to involve the social factors are only of such a kind as to facilitate the approach or access to the person or object which will call forth the tactile response. There is no evidence that the prepuberty child can get any kind of sex satisfaction from sex thoughts alone—it must have the tactile stimulus. Erections seen in young boys may occur from reflex stimuli but not from psychic control.

The curiosities of young children about the sex apparatus of their playmates is of the same order. They are not sex conscious in their investigations but it is reasonable to assume that what is of interest in themselves is of interest in others. This is an intellectual process and arises in the same way as other curiosities. With the formation of new thought associations it is only natural that some of the social experiences will involve associations with the genitalia both of the child and its fellows. No matter how much interest of this kind is shown it does not give rise to sex feeling unless erogenous zones are aroused by touch. And even if two young children should play with each other's genitals it still cannot be said that they are satisfying any bisexual needs, they are merely utilizing a playmate instead of the mother, nurse, or their own hands.

The arousing of any sensation as pleasurable as that resulting from erogenous stimulation may readily become a habit. It is more likely to become so if the act is allowed to be repeated under similar circumstances so that the circumstance itself becomes the conditioning factor that starts off the train of thought toward gratification. Whatever attempts can be made to control the establishment of habits such as handling the genitals, playing "peeping Tom," and sex play between children must take cognizance of the fact that they do these things only because they happen to think about them and not because they feel any sex urge. If there is no local stimulation of sex sensations no true sex impulses will be aroused. Children who have been raised without the sex taboo have minds almost free of such associations and can play naked together without embarrassment or excitation of sex feelings. The distance stimuli cannot initiate sex response at this age.

It is highly desirable to prevent sex habits in childhood because if the habits persist through puberty they are likely to become associated with bisexual activities in such a way as to influence attitudes toward normal gratification. To accomplish this the child should be raised in an atmosphere free from emotional restraint in the interest in sex, and every attempt made to prevent excitation by undue handling, especially during the performance of routines such as bathing, nursing, fondling, and putting to bed. The pernicious practice by child nurses of caressing the genitalia in order to quiet the child is absolutely interdicted.

Little if any notice should be taken of children found in the act of self gratification or indulging together in sex play. Unless much has been made of it previously, what the children are doing is not of very great importance to them, and their attention can easily be diverted by intelligently and quickly interesting them in something else. Young boys frequently masturbate when they are left alone at night to go to bed. The habit arises from self-interest during undressing and bathing and the associated memories of previous occasions when they had aroused sensations in themselves. Now that they are alone it is easy for them to repeat the act. When such a habit has been acquired it is notoriously difficult to break without making matters worse. If the parent adopts the attitude of spying it only drives the boy to subterfuge and exaggerates the importance of the whole affair. They may then become introvertive and make opportunities for self-indulgence. Since these boys are generally old enough to talk to reasonably the best procedure is for the parent who has the most ability to do it without scolding and embarrassment to talk frankly with the boy about it and then ignore it for a long time. It can be done again if necessary but in the meantime, even if the boy continues he will do no particular harm to himself. Accessory measures such as leaving the bed-room door open and the hall light on, and giving him some absorbing interest before he goes to sleep, may be of considerable help in keeping down the habit but can seldom be counted on to break it.

To prevent the habit the most effective measure is to encourage the natural interests of the child. If he can be gotten to think over the activities of the day or to plan for tomorrow, or to perform such feats as imaginative inventions, and making up stories *after* he is undressed and in bed he will most often fall asleep before associations are able to arouse thoughts of masturbation.

The general behavior pattern of children can be so permeated with reactions related to sex that they appear to be primary sex behavior problems whereas actually they have no real concern with sex in the social sense. What they exhibit are complex thought associations acquired by suggestion, mimicry, and imaginative phantasy constructions which they have picked up from stories, observations of the behavior of older boys and girls and adults, motion pictures, illustrations and all other suggestions of human sex relations. Beneath their sex-pretending lies nothing more than emotional response which has no more specific bearing on sex feeling and excitation than the emotions of ordinary adventure and experience. What happens is that some of these associations may bring about situations which result in sex sensations on the purely physiologic level. These children may be interested in sex and want erotic sensations but they cannot get them until *after* the tactile stimuli

have aroused them; they may be sex-minded but they are not sex-conditioned. If this distinction is clear in the minds of those who *attempt to prevent or correct such behaviorism many difficulties of* child training will be avoided.

It is natural for the young child to inquire about what it sees and hears about sex, and it will demand some sort of explanation. But explanation must not go beyond what the child can comprehend and so far as sex is concerned this amounts to almost nothing; it cannot understand bisexual relationships for the origin of babies, and the physical basis of marriage as an explanation of husband-wife behavior would remain a complete mystery to it. The simple questions of children must be answered as simply as they are put, with the precaution not to arouse further curiosity by presenting them with new problems.

Sex shocks in childhood may produce lasting harm by their later *association as memory experiences with actual bisexual relations.* Thus, the young girl who has been attacked sexually and the boy who has been used by homosexual men may have psychic scars which never heal and are the bases of true sex complexes in later life. The minor sex associations of childhood may also remain as causes of sex conflict if the components are sufficiently vivid and emotional when they are aroused by later experiences that can relate themselves to them. With good training most of these latter can readily be disposed of by rational understanding. Efforts to break the sex associations of childhood must be applied coincidentally with the development of true social sex consciousness and the time for this is before or at puberty.

Puberty institutes a new biologic era in child life. It is characterized by active ovulation and spermatogenesis, accompanied by profound changes in the whole psychobiologic unit. Masculinity and femininity become more outwardly apparent in physical structure, growth tempo, and psychic attitudes and responses, but of even greater importance than these are the invisible changes within the organism. The activity of the gonads, pituitary, and other glands of internal secretion, require the establishment of new balances, and the integrating nervous system is strained to participate in the readjustments. The psychic and emotional activities respond to the new order and reveal themselves in desires, behaviors and satisfactions that were unknown to the organism before. In this milieu, sex plays a dominant rôle; it is not only a quantitative increase in sex activity but a new responsiveness to sex needs.

Before puberty sex feelings were purely physiologic in origin. With the appearance of new mechanisms of sex gland activity stimuli other than tactile become able to excite sex-feeling. These distance stimuli, sight, sound, and odor stimulate their appropriate receptor mechanisms and register their effects on the psychic level

as particular feelings. If these feelings have sexual associations the emotions aroused express themselves as usual in vasomotor and secretory responses throughout the body, but in addition now call forth autonomic responses in the genital apparatus by means of the new sex mechanisms. It is even possible for auto-erogenous thought processes to initiate an emotional response that can operate in the same way. The result in both instances is the institution of physiologic states in the sex mechanisms which give rise to imbalances and tensions that have an underlying quality of discomfort. This is the physiologic basis of the sex instinct. It is a need that calls for satisfaction and in the human, satisfaction is gained by deliberate psychic attention to it and the appropriate subsequent behavior reactions.

The pubescent child is a sensitive psychobiologic unit that can respond to external distance stimuli that may be associated with sex and is even sensitive to its own thoughts. In this sensitive state it is not long in recognizing that its own sex feelings are aroused most intensely by the sight, sound, odor or thought of the other sex so that girl and all that pertains to her becomes a symbol of sex feeling for the boy, and the girl recognizes the same response to her opposite.

The behavior that results from this powerful and growing sensitivity will be highly conditioned by past habits and thought associations of earlier childhood. As experience increases in this new state the opposite sex becomes more and more involved. The child cannot at first understand the full meaning of the new symbolism but as knowledge and understanding grow the young adolescent becomes aware of the need of the opposite sex for the satisfaction of its feelings. Bisexual (heterosexual) sexuality is now a reality and the problem which it raises must be solved.

The wide variations seen in the intensity of sex life and interests of individuals cannot be laid to any single cause. To say that they are oversexed and undersexed is a truism. Nor is the overt behavior a true reflection of the real intensity of sex responses within the individual. There are, however, several factors that go to make up the total sexuality. On the physiologic basis, femaleness and maleness are now considered as quantitative aspects of the balance between the female and male hormones. Although primary sex determination is a function of the chromosomes, the phenotype or actualized individual manifests more or less femaleness or maleness as the result of postconceptional gonad and other hormonal influences. The explanation of why the endocrine balance favors male or female secondary sex tendencies is not yet known but developmental changes, resulting from extra-sex factors, may be important. The total result in the individual is to produce average males and females and between them all degrees of female aspects in males and male aspects in females.

On the psychologic level there are females who otherwise appear entirely feminine, but who adopt male attitudes and some of their characteristic behaviorisms, and males are seen who act in a highly feminine manner but do not look feminine. These disharmonious types are highly conditioned by past experiences and training and possess associations that do not conform to their sex potentialities. In many of these there is no need to postulate any physiologic differences in their sex types for a careful analysis of their past history frequently reveals the fact that they have been subjected to social environmental influences that made it expedient to react in certain ways for their own satisfaction; the tom-boy girl may thus carry her masculine ways through puberty and interpret her sex feelings with this boyish coloring.

The third disharmonious type is the young boy or girl of adolescent years who is over-, or underemotional. The emotionalism may be real, as it is in the spoiled tantrum-exhibiting child, or it may be due to constitutional inadequacy of the affective mechanisms, as is suspected as the basis of hysteria. In these boys and girls the emotionalism of childhood becomes confused with the sex-emotion responses after puberty and produces reactions which appear inappropriate to their sex.

In the normally sexed, variability in sex behavior is largely determined by the balance between the acceptance of personal and social values. (The latter are discussed more fully in the next section.) In another place, it was pointed out that what society wants is not necessarily what the individual wants. If the two dictates coincide in an individual's value of sex his sex-behavior will correspond with social acceptance. If, on the other hand, there is little correspondence between the two, the individual has two alternatives; he may repress inwardly and conform outwardly, or he may exercise his individualism and scorn social opinion and even law.

In all degrees of sexness, behavior is largely preconditioned, that is, the individual does not abruptly change over to new attitudes and behavior just because sex references after puberty are made to extra-personal relationships. What values he or she possessed at puberty remain as the accepted values for at least some time during adolescence and may persist throughout the remainder of life.

The culmination of the sex-instinct in sex-experience is the natural biologic course of events but in Western societies is permitted only after marriage. This is a social expediency to prevent chaos in the social problems of personal rights, property, inheritance, democratic representation, taxation, etc. These factors have no primary concern with sex but are involved in it whenever the family is set up as the social unit. In this milieu of intruding factors the primary

biologic urge to mate is faced with a contradiction that it must resolve. It is faced with the need of going ahead in its own individual way or accepting a dielectic course that will conform to social decrees and give some degree of personal satisfaction. In this impasse it is a wonder that all adolescents do not immediately plunge into sex-experience and satisfy their needs completely. *The important question therefore is not why juvenile sex-delinquency occurs* but why it does not in so many instances. It is easy to understand why one youth follows his desires and seeks satisfaction *but it is not always clear why another does not.*

The answer appears to lie in the presence of a number of "checks" on overt sex gratification out of marriage (in Western cultures particularly). These checks are the acceptance by the individual of certain personal and social values; they are neither permanent nor infallible and can be effective only insofar as they dominate any particular situation. A few of them may be mentioned. (1) Family pride. In a survey of medical students taken by the author to find out why those who had never had bisexual relations before marriage, had not done so, family pride was one of the commonest answers. The subjects could not break this concept down into any more definite elements and admitted that it was not necessarily either an intellectual, emotional or sentimental attitude. It was described by them as a general feeling of loyalty to the principles which had always been paramount in their family conduct. (2) Fear. The fear of conception and the fear of venereal disease was the most commonly found check in the same study. Obviously *this is not an intellectual restraint because neither conception* nor venereal disease is a necessary consequence of sex exposure and it becomes even less so with knowledge of contraceptive and anti-venereal prophylactic devices. *Any individual who is at all accus*tomed to taking chances in other aspects of life will not be stopped by the small odds presented by the use of preventive measures. Fear of the ability to consummate the sex act was not included in any of the answers but it is a commonly accepted psychologic restraint. It appears to originate from a feeling of inferiority. *(3) Religion. Some few of the medical students were checked by* religious attitudes toward promiscuous sex indulgence. When religiosity is a strong determiner of behavior there is no more powerful check on liberty of action in sex practices. That it is not complete or permanent is revealed by the innumerable instances of failure made familiar to everyone through confessions made in the church and elsewhere. (4) Social obligations. In the culture of America, at this time, society is opposed to promiscuity and laws are made to uphold the integrity of the family and to prevent the commercialization of vice. One who accepts these dictates may carry them into his social behavior and refrain from acting against

the law and his own conscience. (5) Respect for women. This is an attitude compounded of many elements. It is a high ideal based on a general acceptance of the respect and love which is due to women generally and to the mother and sisters in particular. When it is applied without discrimination to all representatives of the female sex the possessor is not likely to perform any act against one of their number which will, according to his ideal, degrade both her and himself. (6) Self-esteem. This is put on many levels. There are young men and women who understand the fundamental principles of sex and reserve to themselves the right to be particular in the exercise of the sex function. There are some who feel degraded by giving in to a desire which does not have to be gratified at this time. Many delay the first experience until it can be consummated with a particular mate whom they expect to choose as a life partner and feel that they would be cheating themselves out of a supreme delight in spoiling it with a non-love mating. Finally there is the shy, fearful individual who feels that he or she could not enjoy the consummation unless everything concerned was ideal; such a person is living in a fairy story existence and would probably be disappointed under the best conditions.

The subject has been sufficiently reviewed to indicate that sex-behavior is largely a matter of sex-thought conditioning. When it becomes necessary therefore to take positive steps to direct sex-behavior in order to prevent delinquency, perversion, etc., careful consideration must be given to the motivations underlying not only the observed reaction tendencies but also the inner associations that direct them. The parent, teacher, physician and religious adviser are all in a position to inculcate intellectual associations that lead to rational behavior in sex matters. None of the attitudes described above are fixed and unchangeable. It may be difficult to alter habit thoughts and to erase complexes but it is not impossible. It is far easier to try to understand children and train them according to their particular types and tendencies in the expression of even so private and personal an affair as sex.

Sex symbolization becomes so diffuse for some people that almost every situation contains some sex element or some association that can be related to sex. These are the constantly sex-minded types but they are not necessarily excessively sex-behaving. They, like all others, have only their particular likelihood of translating sex thought into sex action. They are, however, always in danger of having their intellectual processes and personal values interfered with by the importunity of sex associations, and the association habit is therefore undesirable from the point of view of balance in the whole personality.

The solution of the problem of sex satisfaction is seldom possible without some conflict. Suppression to some degree is essential in a

cultural community where sex promiscuity is taboo on any level whether legal, religious, moral, ethical, or unexpressed social custom. The conflict between necessary suppression and overt sex-behavior can be solved by continence and complete celibacy, the adventurous indulgence in occasional sex gratification, or by marriage. When one of these logical solutions meets with contradictions within the circumstances of their practical application, further adjustments become necessary. Continence may become intolerable, casual gratification may not be satisfactory, and marriage may not bring forth the ideal adjustment hoped for. These are serious set-backs to desire and if the normal desire cannot be obtained by a new dielectic which introduces changed attitudes and altered values there is always the possibility that the individual may adopt even more unsatisfactory solutions commonly referred to as perversions. Perverts are made and not born. Even though inborn or constitutional defects exist which make normal sex acts impossible or uncomfortable they do not necessarily lead to perversion. The perverted sex act is the outward expression of psychic factors which have altered the personal values and their consequent behavior trends; they are the results of poor dielectics and as such must be looked upon not as disease but as correctable disorders of psychogenic origin. This conception makes it possible not only to cure perversion but to prevent it. A proper understanding of the conflicts involved, with knowledge of the altered attitudes and values which enable them to be actualized in perverted behavior, should permit outside interference through teaching and training, and providing for normal outlets by environmental readjustment.

The selection of a life mate does not necessarily mean the solution of sex problems. Ideally it should, for selection is generally voluntary and personal and involves a mixture of intellectual appreciation of the virtues of the partner as the chooser sees them, and an emotional attachment that arises from the symbolization in one partner of all that the other considers most desirable. In addition there are the appreciations of like interests, similarities of tastes, complementary abilities, skills and potentialities, and the economic probabilities of a successful match. Actually, this ideal is seldom realized completely and the happy marriage is full of dielectic by-paths on the part of both partners—commonly called compromises. The part played by sex in this perilous adaptation is great. It must not and cannot afford to dominate the situation entirely because of the immense variability in the desires of the partners from time to time, and the necessary interruption of gratification during periods of separation, menstruation and late pregnancy. No marital union can be permanently satisfactory to both partners if sex is the main consideration all of the time and possibly for even the greater part of the time. Sex technics in marriage are not difficult to

master on the physical level but are notoriously so on the psychic level. Intelligence, control of the emotions, eradication of unrelated sex associations carried over from the pre-marital life and the cultivation of frank, mutual understanding between husband and wife as to each other's problems in regard to sex gratifications, make the best insurance for marital accord.

In conclusion, a word must be said about continence. The medical profession has declared its disbelief in any physical harm resulting from continence. Psychic harm may result if continence is not in harmony with the inner values of the individual because it results in painful repressions and psychic perturbation. The advice to young men that sexual intercourse is physiologically necessary is as faulty as to tell them that they should have sex experience before marriage so that they will be better experienced when they have taken on the responsibilities of a life partnership. Sex relationships before marriage, unless they are carried out with the same affectional attachments as in marriage and without social and personal restraint can be of little help to the intended husband or wife. Promiscuous experiences outside of marriage are seldom with virgins, they are without responsibility, and there is little or no real affection involved. This is quite the opposite from the bride and groom relationship. What is needed far more than physical experience is sympathy, tact, understanding, and personal control.

TRAINING IN THE ACCEPTANCE OF SOCIAL VALUES.

Because man can only exercise his full function by participation in a social group the social relationship becomes as important to his existence and welfare as his internal psychobiologic integrations. Social values are functions of the group relationships and therefore, insofar as they influence the individuals of the group, constitute the biosocial factors of their environment. These factors are unavoidable and the success of the individual rests largely on his ability to adapt himself to them. On the psychic level this means the conscious acceptance of the values and voluntary adjustment to them.

Gesell has expressed the keynote of this acceptance when he says "the individual must repress, in order that another may express." This is difficult to accomplish when the individual is of the aggressive, ambitious, individualistic type, and is overdone in the retreating, shy, fearful, and overmodest. The intermediate type is more successfully adapted but relatively uninteresting and probably does not contribute as much to human progress as the less well adapted. The aim is therefore not toward a static neutral adaptation, but individual conformity to the laws of society within the limits of successful adaptation.

The conflicts between individualism and social conformity arise

immediately after birth with the first expressions of dissatisfaction by the infant at the way in which others fail to comply immediately with its demands. Through conditioning, the baby's demands become timed and less importunate, and thus a passive adjustment is attained which is satisfactory to all concerned. This process goes on in many activities until the time arrives when ideas, thought associations, and voluntary behavior responses come into control and meet with the equally demanding responses of others. Many of the resulting conflicts have been enumerated in the preceding discussions of the instinctive needs, emotions, intellect, and sex. Running through the responses in each of these categories, there have been conflicts, frustrations and successes, and in each the *necessity of some solution to the problems aroused has been indicated.*

The real give and take of life begins with play between children. In the earliest associations of play, children learn that everything is no longer on their side but that each one wants the red ball at the same time but only one of them can have it. The little red ball and the solution of the problem of who will get it, and how, and why, typifies all social relationships.

Beneath each problem lies the individual's desire to succeed. This, according to Adler, is the prime motivator of human behavior because it is an elemental need which demands satisfaction. That "nothing succeeds like success" is one of the earliest lessons learned in social behavior, but this is quickly followed by the knowledge that success is not an invariable consequence of desire. To circumvent this apparent impasse the device of indirection is soon discovered so that even outward failure becomes inward success. On this basis everyone succeeds, but at a price.

The implications in this brief picture of struggle and success are many. In the first place it is important that the desire to succeed cannot be permitted without giving some consideration to the desire by others to succeed. The "well brought up child" has learned his first implication, the "spoiled child" has not. This does not mean that the first child is any more negative and supine than the over-*indulged second; it is certainly better adapted and, in the long run,* has the greater success. Bringing the child up properly, in this respect, is not "breaking its spirit," "holding it down," "ruining its individuality," or any of the other absurd generalizations made about the process. It is training the child to understand that it is only one member of society and that all others have rights equal with its own; that everyone cannot have everything at once and compromise must be made somewhere; that such things as thoughtless interruption of others' important activities, destruction of property, smartness of behavior and showing off, disobedience for unreasonable purposes, overemotional demands, sulking and im-

pertinence, and whining, cringing, or spineless responses to correction, are not cute, pleasant, good-mannered traits, and under many circumstances are intolerable. The opposites of these undesirable traits can be attained by giving calm, considerate and thoughtful consideration to the minutiæ of behavior as it is being formed in the cradle and the playroom. The program at these earliest ages does not call for interference with the child's attempts to satisfy its desires as much as it does an intelligent arrangement of the environment so that successes and failures are well distributed, and the emotional elements are not aggravated. Children soon learn to take disappointments caused by other children with whom they can cope on even terms. They must be expected to fight and quarrel for this is their only defense. In time they learn to appreciate the social value of give and take, but in the early years it is nothing more than an emotionally conditioned pattern of behavior.

When the child starts its schooling it is harassed by a multiplicity of contacts and conflicts and is expected to meet them without the support of mother or nurse. Frustrations and successes become more accentuated, and frequently the former may be so acute as to send the child scurrying back to the protection of the home. Extreme tact is required in the handling of such cases. To be oversympathetic and protecting too often results in prolonging dependence on the mother, and the child thereby finds a new avenue toward success. If undue harshness is directed toward the unadjusted child it will seek satisfactions in far more undesirable ways such as indulgence in excessive emotional outbursts, disobedience, frank refusal to return to social contacts, or belligerence. The principal on which such children must be dealt with is that of compromising with the child in the present situation so that no vindictiveness will be aroused and the whole episode will be passed over with as little permanent associations with the event as possible. The child should be accepted on its own level, not coaxed or cajoled, but at the same time not made to feel too comfortable about its temporary victory.

One of the commonest devices of children to attain success is by coöperative effort. Every classroom, playground and neighborhood group is a scene of shifting alliances to suit the needs of the moment. Where one child cannot gain its point, two of them working together often can. This is the anlage of group action, gangs, and similar youthful and adult associations. But in early and even late childhood the integrity of the group is never assured from day to day; they are expedient adherences for temporary purposes only.

Toward late childhood, leadership usually springs up and exercises its authority by virtue of better physique, skills, or more

aggressiveness. Bullying is the exemplification of this in a more extreme degree. Conditioned associations of all sorts originate in these associations. They are manifested by submission to leadership, hero-worship, crushes, self-effacement, suggestibility, the take-a-dare attitude, mischief-making, and under older leadership, by the formation of gangs of young vandals, truants, delinquents, and juvenile law-breakers.

When the same tendencies are directed into more constructive channels they produce teamwork, group spirit, coöperative efforts in constructive activities such as clubs, combined craftsmanship, group interests in nature study, camping, drilling, and the many character-building institutions created by modern society to sublimate the energies and interests of children into worthwhile efforts.

It is within the juvenile associations that the individual personality first meets with the obligation to accept or reject the responsibilities imposed on him by the ethnic and cultural elements of his environment. Although some responsibilities have been faced within the family and the home, the intensely personal aspects of this relationship protect it from most of the competitive spirit and unsympathetic attitudes of the outside world. In the home, obedience to parents and adjustments to the wishes and commands of other members of the household are paramount, but in the school and on the street the child is face to face with law and order and social acceptance; it meets too with the culture of its society and learns something of the meaning of such social facts as community interest, the arts, work, the value of education, the desirability of training in particular skills, ethics and esthetics, the force of law and compulsory restrictions, opportunity, group loyalty, ideals of social conduct in manners and appearance, the value of human life, the importance of health and inefficiency of sickness, cruelty, squalor, penury and want, riches, success of individuals, religious attachments and rituals, and the attitudes of others about them.

In an amazingly short time, the young girl and boy has run the gamut of most of the social values. Some have made no influence on them at all, others have affected them temporarily, and a few have made lasting impressions on their feelings and attitudes. As acquaintance with the social elements increases, the child, already an active, participating member of society, is forced to some acceptance of their inevitability and must adjust itself in some way to them; it cannot remain neutral. How it will accept them is determined largely by its own personal values which are certain to be affected. It is for this reason that training in the personal values should antedate guidance in their acceptance or rejection, and therefore some degree of training in control of the emotions is good preparation for the conflict with social values. Altogether, it is a question of

the total personality faced with situations to which it is expected to act in more or less conformity with the attitudes of the time and circumstances.

The whole problem of social adjustment is included in the general terms, *obligation* and *responsibility*. As a unit of society, the individual must possess each of these to a greater or less degree; the personality is forced to compromise with its social environment as much as it is required to regulate its food and exercise in keeping with its best interests. How much compromise will be necessary cannot be determined beforehand. Individuality of thought and action are necessary for personal satisfaction, and since this satisfaction will be gained at any price it is best that it be guided in at least all of the major acceptances.

Where adaptation has gone awry there is likely to be delinquency, criminality, cruelty, lawlessness, withdrawal from society, suicide, and other undesirable solutions too numerous to mention.

Sound appreciation of education, self-control, individuality of expression within broadly accepted limits, constructive attitudes by the individual for the good and advancement of society, are the reasonable and intelligent solutions to be held out to the child and youth who is growing in and with society. If these are implanted on a foundation of high personal values, with good health to back them both up, there will be fewer maladjustment problems to fill the guidance clinics, reformatories, prisons and institutions for the mentally disordered.

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